X JORNADA DE JÓVENES INVESTIGADORES DEL I3A

Collagen Density Regulates Tumour Spheroid Growth Through Cell Motility: A Computational Study

Inês G. Gonçalves, Jose Manuel García-Aznar

iggoncalves@unizar.es, jmgaraz@unizar.es

Instituto Universitario de Investigación de Ingeniería de Aragón
Universidad Zaragoza

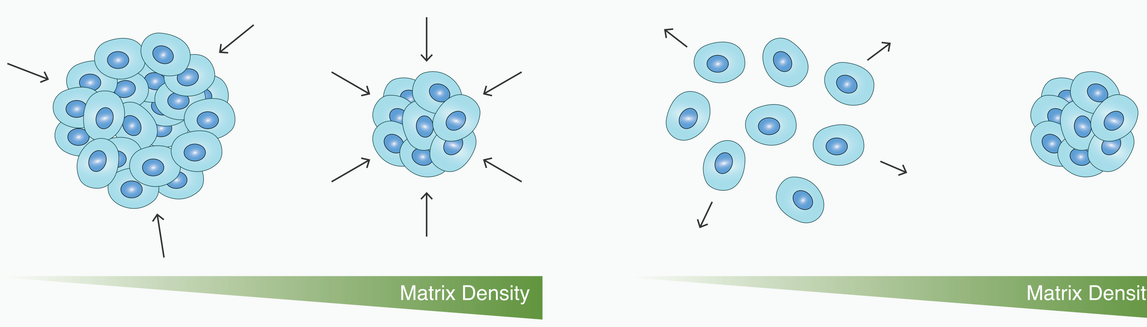
ABSTRACT

We aim to define the role of matrix density on tumour growth through a discrete computational framework. We integrate experimental data to characterize the dynamics of individual cellular movement, accounting for the mechanical properties of the ECM, and we evaluate how the emerging trends modulate the growth of multicellular structures.

INTRODUCTION

Recently, several studies have revealed an interplay between the mechanical properties of the extracellular matrix (ECM) and the emergent cell behaviour.

Studies have shown distinct responses to the properties of the ECM:



Growth supression (steric hindrance) **Cell movement inhibition**

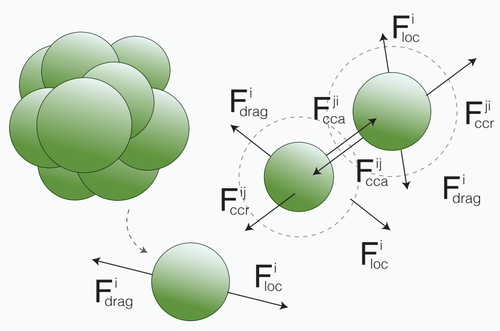
We present a discrete computational model, calibrated with previously published experimental data on cell motility and cluster growth.

METHODS AND MATERIALS

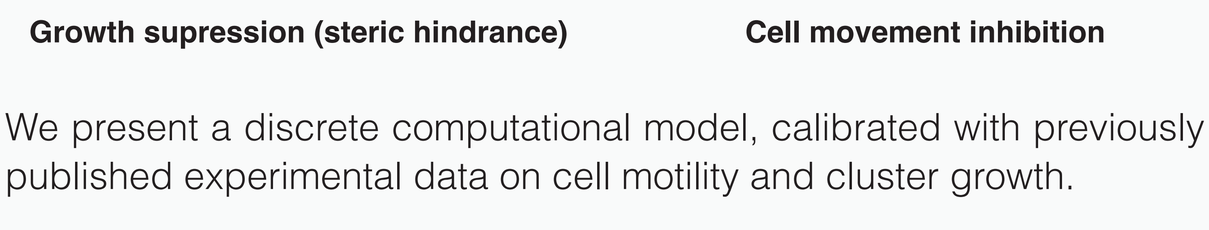
- Model based on the open-source framework PhysiCell;

- ECM properties introduced through empirical dynamic viscosity values;

- Cell-generated forces estimated from experimental velocity values through Inverse Transform Sampling;



Model force diagram

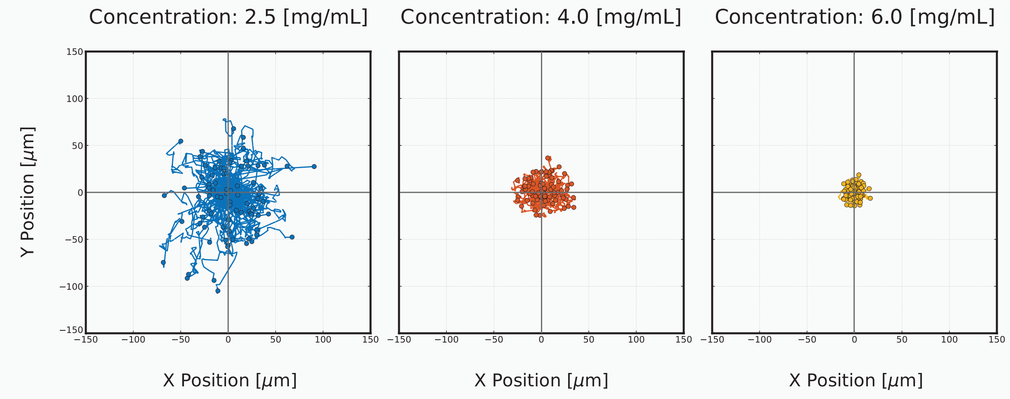


Locomotive forces generator function based on inverse transform sampling

We replicated experimental studies that focused on individual cell motility. Subsequently, we used the calibrated model to predict growth.

RESULTS

We simulated the individual motility of cells in three different collagen concentrations. Overall, our results show that migration was suppressed by the matrix density.

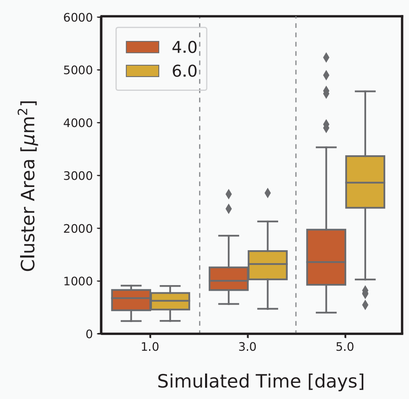


Trajectories of individual simulated cells over 24 hours

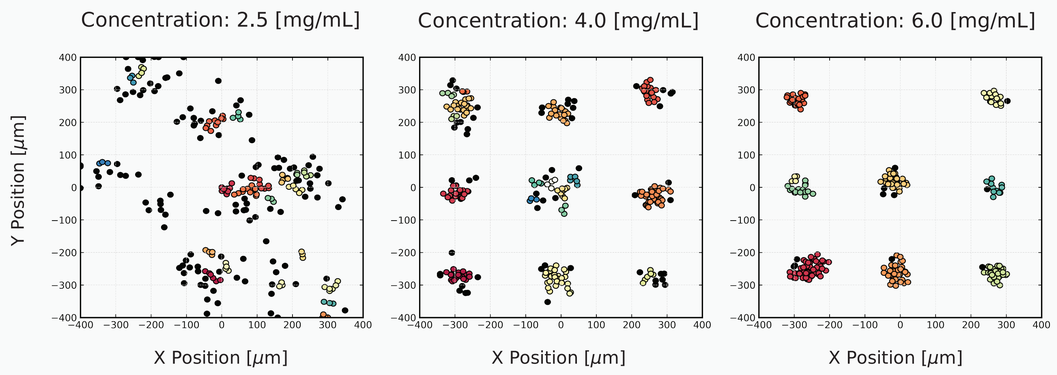
Cluster growth was assessed to characterize the formation of multicellular structures over time.

No significant structures were formed at low density values.

Furthermore, matrices of higher density promoted cluster growth.



Cluster area over time



Cell positions at 5 days. Colors represent the cells' clusters

CONCLUSIONS

Our model describes how an increase in matrix density produced smaller cell velocity values, suppressing the invasion of single cells.

When cells were unable to migrate, they produced large cell clusters. In contrast, lower density values enable cell migration, resulting in sparser and smaller tumours.

Aknowledgements
This work was supported by the European-funded CADENCE project (No. 742684), the PRIMAGE project (No. 826494), the Department of Science, University and Knowledge Society of the Government of Aragon (T50_20R), and the Spanish Ministry of Science, Innovation and Universities (RTI2018-094494-B-C21 and PRX18/00147).

Scan me!
Get the full publication by scanning this QR code with your phone.

Multiscale in mechanical and biological engineering