

Dynamic computational models of cell-extracellular matrix and cell-cell interactions

Citation for published version (APA):

Karagöz, Z. (2024). *Dynamic computational models of cell-extracellular matrix and cell-cell interactions*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20240109zk>

Document status and date:

Published: 01/01/2024

DOI:

[10.26481/dis.20240109zk](https://doi.org/10.26481/dis.20240109zk)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Valorisation

The shift towards functionalized materials in tissue engineering began to gain prominence since the beginning of this century. Researchers realized that mimicking the dynamic and interactive nature of the native tissue microenvironment was crucial for successful tissue regeneration. This involved considering the biochemical, mechanical, and topographical cues that cells experience in their native environments. The goal was to create materials that could recapitulate the complex cell-matrix and cell-cell interactions observed in natural tissues, thus improving the regenerative capacity of cells, tissues and organs.

The ambitious aim of mimicking native tissue environment requires thorough understanding of cellular biology with all the reciprocal feedback between cells and their environment. Computational biology has been a crucial tool for tissue engineering and regenerative medicine by providing valuable insights, predictions, and guidance throughout the process. The computational models presented in this thesis contribute towards understanding the fundamental biological processes and predicting cell behavior. They can simulate and analyze the interactions between cells and between cells and their surrounding extracellular matrix (ECM). By integrating experimental data and existing knowledge, these models provide a deeper understanding of cellular adhesion (**Chapters 3, 4**), signaling pathways (**Chapter 5, 6**), and tissue development (**Chapter 6**). This information will help tissue engineering and regenerative medicine fields in designing optimized scaffold materials culture conditions with optimum stiffness, ECM mechanical properties and integrin/growth factor receptor targeting peptides predicted using the models in this thesis. Eventually, the aim to guide cell behavior towards desired outcomes will be one step closer.

The area that encompasses the utilization of personalized physiological computer simulations in every aspect of disease prevention, diagnosis, prognostic evaluation, treatment, and biomedical product development is termed "*in silico* medicine". In the future, the computational models in this thesis could be incorporated into bigger frameworks of *in silico* medicine as they have the capacity to be used for virtual testing and optimization of tissue engineering methods. *in silico* medicine is gaining more and more attention as global healthcare systems face the challenge of increasing de-

mand and costs. The need for scaling up the personalized treatment options as well as making them more accessible is also increasing (Lesage *et al.*, 2023). Computational biology and experts in this field are highly valuable in making *in silico* medicine applicable in the clinic. A report by the Virtual Physiological Human Institute (VPHi, <http://www.vph-institute.org/>) demonstrated the increasing confidence of clinicians on *in silico* tools for medical planning and prediction. Yet they have also indicated the difficulties in accessing up-to-date computational applications and proper technical expertise in the field of *in silico* medicine (Lesage *et al.*, 2023). These difficulties can be overcome by initiatives like VPHi with the support of national and global support. Recently, European Medicines Agency (EMA, <https://www.ema.europa.eu/en>) announced a work plan for increasing the utility of big data in regulation, to empower data-driven medicines regulation in the European Union. Similarly, The United States Food and Drug Administration (FDA, <https://www.fda.gov/>) agency has formed a Modeling and Simulation Working Group to focus on improving the use of computational models in addition to traditional methods for *in vitro* testing and *in vivo* studies. In summary, in the future, computational models like in this thesis will be used (with modifications) in predicting cell behavior, scaffold design and optimization and virtual testing and optimization of *in silico* medicine tools.

References

- Lesage, R., Van Oudheusden, M., Schievano, S., Van Hoyweghen, I., Geris, L., & Capelli, C. (2023). Mapping the use of computational modelling and simulation in clinics: A survey. *Frontiers in Medical Technology*, 5.