

## Modeling the development of tissue engineered cartilage

***Citation for published version (APA):***

Sengers, B. G., Oomens, C. W. J., & Baaijens, F. P. T. (2001). *Modeling the development of tissue engineered cartilage*. Poster session presented at Mate Poster Award 2001 : 6th Annual Poster Contest.

***Document status and date:***

Published: 01/01/2001

***Document Version:***

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

***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.tue.nl/taverne](http://www.tue.nl/taverne)

***Take down policy***

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

[openaccess@tue.nl](mailto:openaccess@tue.nl)

providing details and we will investigate your claim.

# Modeling the development of tissue engineered cartilage

B.G. Sengers, C.W.J. Oomens, F.P.T. Baaijens

Eindhoven University of Technology, Department of Biomedical Engineering

## Introduction

The composition of tissue engineered (TE) cartilage depends to a large extent on the bioreactor configuration, see figure 1. The EU project IMBIOTOR aims at realizing an intelligent bioreactor in which the properties of the TE construct can be tailored using model based control of the complete bioreactor environment. Manipulating global input parameters: Nutrients, growth factors,  $O_2$ , pH, temperature, time and mechanical stimulation, will yield the local output: Collagen II, proteoglycans, cells, permeability and stiffness.

## Objective

- A numerical model that can predict local construct properties as a function of the global input.

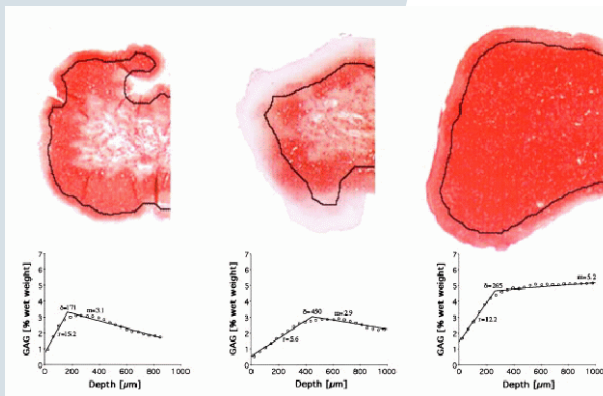


Figure 1 GAG (Matrix) distribution for constructs cultured in static flasks, mixed flasks and rotating bioreactors [1].

## Methods

A description of highly coupled phenomena, like mechanical adaptation, solute transport, cell growth and biosynthesis is required, which has to deal with quantitatively ill-defined chondrocyte responses. Figure 2 shows the proposed model.

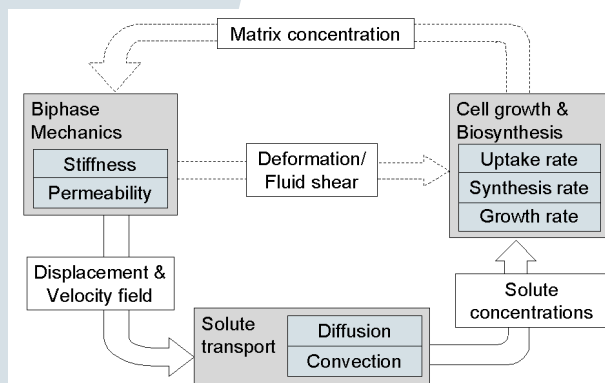


Figure 2 Proposed model.

A biphasic description captures deformation and mechanically induced convection, ignoring electro-osmotic effects. Simple unstructured kinetics for nutrient uptake, cell growth and biosynthesis will be used [2, 3]. Kinetic rates are influenced by cell and matrix content and nutrient availability. A deformation measure can be used to account for direct mechanical stimulation. The resulting matrix concentration will determine the permeability and stiffness.

## Results

Figure 3 shows examples of the model's possibilities.

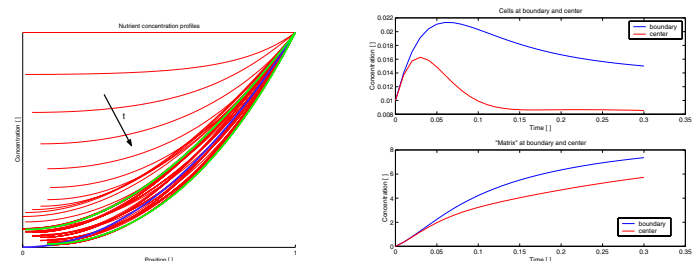


Figure 3 Left: Nutrient concentration profiles for cyclic deformation in confined compression and constant nutrient uptake. Green are the constant limits reached after a number of cycles. Blue is the steady state profile without deformation. Right: Cell and matrix concentrations in the center and at the boundary (no deformation).

## Conclusions

- Further integration of models for mechanical adaptation, solute transport, cell growth and biosynthesis will lead to significant progress in controlling the development of tissue engineered constructs in bioreactor culture.
- A biphasic model is proposed with local permeability and stiffness depending on matrix synthesis and cell growth, which are influenced by deformation and nutrient transport.
- The present model gives a qualitative picture that has to be quantified and validated using experimental data.

## References:

- [1] I. MARTIN, B. OBRADOVIC, L.E. FREED, G. VUNJAK-NOVAKOVIC: *Method for quantitative analysis of glycosaminoglycan distribution in cultured natural and engineered cartilage* (Annals of Biomedical Engineering 1999, 27, 656-662)
- [2] B. OBRADOVIC, J.H. MELDON, L.E.FREED, G. VUNJAK-NOVAKOVIC: *Glycosaminoglycan deposition in engineered cartilage: Experiments and mathematical model* (AIChE Journal, 2000, 46-9, 1860-1871)
- [3] C.J. GALBAN, B.R. LOCKE: *Effects of spatial variation of cells and nutrient and product concentrations coupled with product inhibition on cell growth in a polymer scaffold* (Biotechnology and Bioengineering, 1999, 64, 633-643)