An integrated finite element approach to mechanics, transport and biosynthesis in tissue engineering

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Introduction
In order to reach the stage of clinical applicability a definite need arises for improved control over the functional properties and composition of tissue engineered cartilage constructs. The EU project IMBIOTOR aims at realizing an intelligent bioreactor using model based control. Within the project our objective is a numerical framework that relates global biochemical and mechanical bioreactor input to local functional tissue development. To illustrate the approach the synthesis and transport of matrix macromolecules (GAG) is investigated with and without cyclic compression [1].

Methods
A non-linear biphasic displacement-velocity-pressure (u-v-p) formulation is implemented. Computed displacement and velocity fields are used for advective and diffusive transport of an arbitrary number of solutes. Solute concentrations determine cell behavior, see Fig. 1. For flexibility solute uptake is included using operator splitting.

GAG biosynthesis is modeled using a modified relation based on local oxygen tension [2]. No assumptions on direct mechanical stimulation and adaptation of permeability and stiffness as a result of matrix deposition are included in the present study. The analysis is kept one-dimensional at first.

Results
Computed fluid velocity profiles due to low frequency (0.0008 Hz) cyclic loading are smooth and after a few cycles the solutions become approximately periodic. Figure 2 shows the computed GAG profiles. The center contains less GAG due to nutrient transport restrictions on biosynthesis. For the case of cyclic loading the effect of consolidation on cell concentration leads to increased GAG in the center, compared to the unloaded case.

Accurate multidimensional porous flow calculations will require the use of special elements spaces or stabilized methods [3], see Fig. 3.

Discussion

- The high level of coupling between mechanical and biochemical factors in functional tissue engineering requires an integrated modeling approach.
- Matrix macromolecule distributions can be predicted in qualitative agreement with experimental results [2].
- Stabilized mixed FE methods will be investigated for accurate 3D porous flows in deformable media.
- Comparison with experimental data is required for model validation and for establishing better quantified relations for cell behavior.

References: