Computer-aided tissue engineering of articular cartilage with a physiological collagen architecture

Computer-Aided Tissue Engineering of Articular Cartilage with a Physiological Collagen Architecture

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General Project Introduction

Importance: Articular cartilage damage is a common pathology for which no satisfactory treatment exists. A promising solution is to use tissue-engineered cartilage. However, the load-bearing capacity of today's tissue-engineered cartilage is insufficient.

Hypothesis: We hypothesize that the major shortcoming is related to the collagen content. Both the quantity and the quality are insufficient; the physiological collagen organization, optimal for mechanical load-transfer (figure 1), is not reproduced. The premise is that developing cartilage adapts to its mechanical environment. If this is true, it will be possible to tune the mechanical properties by applying appropriate loading regimes during culture.

Aim: To design loading protocols by which tissue-engineered cartilage would develop a physiological collagen structure.

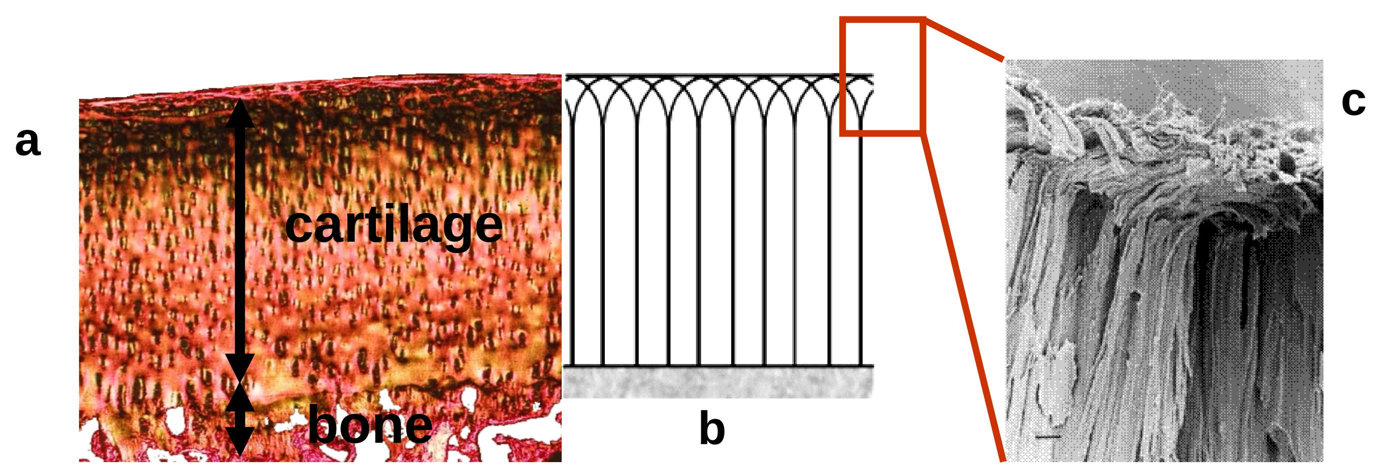

Figure 1: Images Showing the arcade-like collagen structure. a) polarized microscopy of full-depth cartilage slice; b) Schematic representation of arcade-like organization [1]; c) SEM image of collagen structure near cartilage surface [2].

Approach

We adopt a computational-experimental approach, in which computer simulations in parallel with experiments should result in targeted optimization of the loading regime and culture protocol. This will reduce the number of time-consuming trail-and-error type of experiments and improve the ultimate result (figure 2).

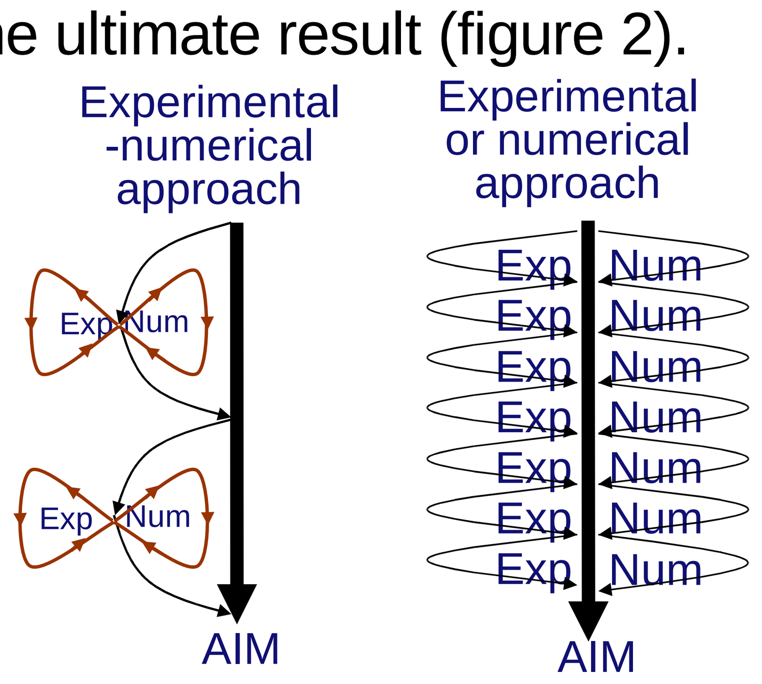

Figure 2: Design of the study to reach the defined aim. Left: Experimental-numerical approach; right: Experimental or Numerical approach

Computational Part

Using computer simulations, we aim to optimize the loading regime, such that the desired collagen architecture develops. Therefore we identified three subgoals:

Aim 1. Describe the mechanical behaviour of the tissue-engineered cartilage throughout the culture;

Approach We use a fiber-reinforced poroviscoelastic swelling model of cartilage [3].

Aim 2. Predict the organization of the developing collagen network;

Approach We adopt collagen-remodelling algorithms (figure 3) [4,5] that can predict the collagen architecture in various tissues, given the external loading conditions. In these algorithms, collagen fibrils are assumed to align with a preferred fibril direction situated between the positive principal strain directions.

Predictions will be correlated with experimental observations.

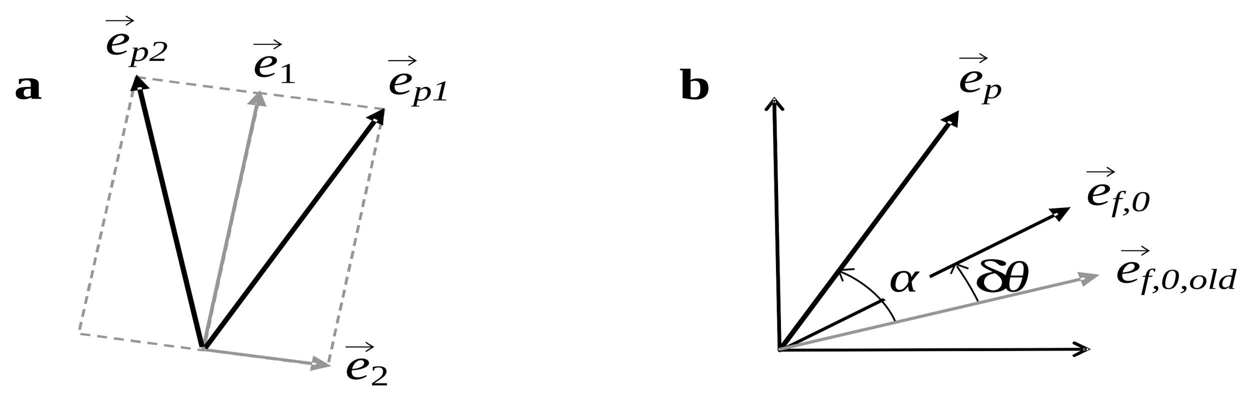

Figure 3: a) The preferred fibril direction e_{pi} is situated in between the positive principal strain direction e_1 and e_2. b) The fibril direction with respect to the undeformed configuration $e_{f,0,old}$ is rotated towards the preferred fiber direction e_p over an angle dθ to result in the new fibril direction [5].

Aim 3. Simulate tissue development over time during the tissue engineering process;

Approach Tissue properties change with time of culture. This will need to be accounted for in order to appropriately predict collagen development in time. This requires algorithms by which culturing conditions are correlated to tissue development. These will be derived from experimental data in the second part of the project.

References

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[2] J.M. Clark, J Orthop Res, 9:246-257 (1991).

[3] W. Wilson et. al, J Biomech, 38:1195-1204 (2005).

[4] J.B. Driessen et. al, J Biomech Eng, 125:549-557 (2003).

[5] W. Wilson et. al, Osteoarthr Cartilage, 14:1196-1202 (2006).