Stem cell mechanoadaptation and scaffold design optimization

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Introduction
With the elderly population rising and athletes pushing their bodies towards limits that have never been explored yet, tissue failure occurs more often than ever. The soft tissue repair global market is expected to reach $21.3 billion by 2023 [1], whereas more than two million bone grafts are conducted every year worldwide [2]. In this context, tissue engineering offers great solutions of repair thanks to auto-, allo- and xeno-grafts. Nevertheless, these grafts face inherent drawbacks as shortage, low biocompatibility and potential for disease transmission. This research thus aims to optimize scaffold designs for engineered tissue with regards to stem cell mechanoadaptation.

Stem cell mechanoadaptation
To assess the stem cell adapting morphology, mesenchyme stem cells (MSCs) were seeded following distinct protocols, at different densities that are low, high and very high density, and on both normal dishes and ones coated with a suitable compliance substrate (polydimethylsiloxane PDMS) to account for mechanical forces acting within the extracelular compartments of the cells in a more realistic way. The shape of both MSCs cytoplasm and nucleus were determined by normalizing the ratio of their surface area and volume by an isovolumetric sphere.

Based on both the virtual power and dissipation principles, MSCs bulk modulus evolution could be evaluated, assuming stem cells are homogeneous linear isotropic materials.

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d_K = \beta^p - \beta^\nu_K, \quad \text{where} \quad \beta^p = \frac{1}{2} I_1^p \quad \text{and} \quad \beta^\nu_K = \frac{2}{\nu} (\frac{p}{K})^\gamma
\]

\(I_1\) and \(p = \frac{3}{2} K \nu\) being respectively the first invariant of the strain tensor and the hydrostatic pressure computed thanks to linear elasticity theory. The evolution seems to be consistent with biophysical behavior as it converges towards a steady state. MSCs stiffness either increases or decreases depending on the remodeling stimulus. Note that this was observable for MSCs seeded on both substrates as well as cells modeled as viscoelastic material thanks to Maxwell model.

At a longer length scale, cellular movements resemble random particles in a fluid. Thus, the diffusion-convection governing equation can be applied to approximate MSCs behavior by which they migrate and proliferate on substrates such as tissue culture well. The proliferation could be compared to measurements in culture well. The migration process was also shown to differ when the MSCs are seeded on normal dish, coated dish (right) or PDMS coated dish (right).

Scaffold design optimization
The scaffold designs were inspired by marine plants such as the Euplectella aspergillum Okeanos. By reproducing cubic features of different porosity in a linear pattern, they were build to mimic dimensions of a cranial defect tissue template from a previous study.

In order to drive stem cells towards the targeted phenotype, CFD and FE studies were conducted to analyze scaffolds performance through permeability, wall shear stress and mechanical strength.

Conclusion
MSCs adaptation is eventually driven by energy costs minimization, whose process triggers specific phenotype. Thus, tissue engineering should benefit from stem cell mechanoadaptation knowledge to optimize scaffold design according to its targeted in vivo application as well as to emulate native tissue environment and mechanical properties.

References