# Computational bone tissue engineering: from carriers and culture to clinics

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One of the major challenges in tissue engineering and an essential step towards successful clinical applications is the translation of biological knowledge on complex cell and tissue behavior into predictive and robust engineering processes. Computational modelling can contribute to this, among others because it allows to study the biological complexity in a more quantitative way. Computational tools can help in quantifying and optimizing micro-environmental signals to which cells and tissues are exposed and in understanding and predicting the biological response under different conditions.
A wide variety of model systems has been presented in the context of tissue engineering ranging from mechanistic models (hypothesis-based) over gene network models to empirical models (data-driven), targeting processes at the intracellular over the cellular up to the tissue level. Each model system has its own benefits and limitations which delineate the context in which it can be used. Whereas mechanistic models are used as in silico tools to design new therapeutic strategies and experiments, empirical models are used to identify, in large data sets, those in vitro parameters (biological, biomaterial, environmental) that are critical for the in vivo outcome.

In this presentation I will show a number of examples of these models (cfr figure 1). The first one being that of biomaterial design. In order to optimize bioceramics-based biomaterials for bone tissue engineering, we have developed models simulating the degradation of the biomaterials upon in vivo implantation, as well as the influence the degradation products have on the local biology. Extensive screening experiments have guided the model formation. In turn, the model is used to predict the bone formation capacity of bioceramics-based biomaterials in combination with a specific cell source.
For the culture of tissue engineering constructs composed of cells and carriers, bioreactors are used. In order to follow-up the biological events occurring inside the bioreactor, computational models are of great help. We have developed a model capable of simulating neotissue growth in perfusion bioreactors, including the influence of scaffold geometry, fluid flow, oxygen and lactate on the speed of growth.
A last example will briefly touch upon the possibilities of computational models in assessing the in vivo effect of specific treatment strategies for bone regeneration. We have developed a model of in vivo bone regeneration with a thorough description of the role of angiogenesis and we are currently testing the effect of a variety of patient properties (defect size, type of trauma, congenital problems) on the regeneration outcome.

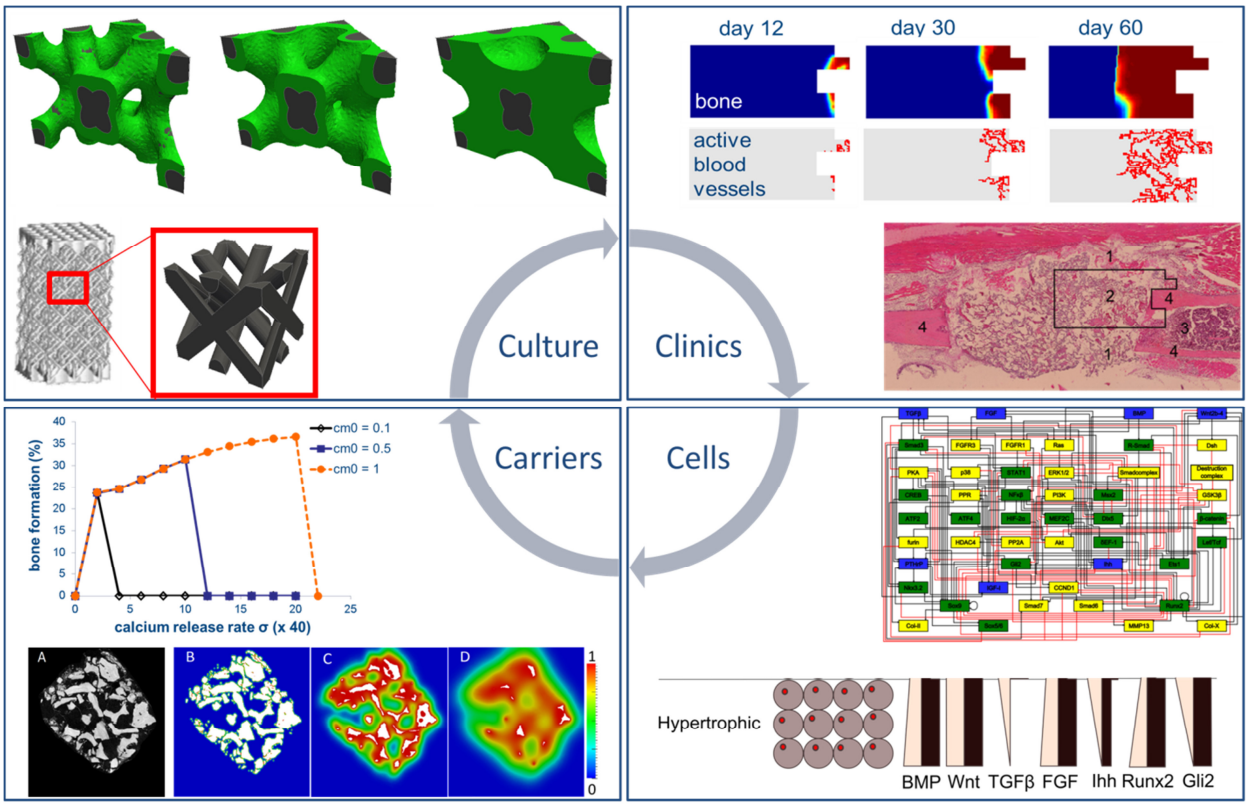


Figure 1: Classification of in silico models by their contribution to the basic building blocks of regenerative medicine [1]. Cell: a gene regulatory network for chondrogenic differentiation is shown, along with a comparison between experimental (pale pink) and simulation (black) results for the hypertrophic phenotype [2]. Carrier: prediction of calcium dissolution from calcium phosphate-based carrier (bottom, unpublished results, courtesy of V. Manhas) and prediction of optimal cell-carrier combinations for various initial cell densities (cm0) [3]. Culture: neotissue (green) growth in a porous titanium scaffold (grey/black) [4]. Clinics: simulation of blood vessel formation in a large defect in mice [5]

References

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