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PARAMETERISED MATHEMATICAL MODEL OF OSTEOBLAST KINETICS IN A STATIC MICROCARRIER CULTURE

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Summary: Tissue engineering is a promising bone trauma treatment when the self-regeneration process is impaired due to extensive trauma or compromised by diabetes or osteoporosis. Tissue engineering and cell therapies have the potential to deliver clinically-relevant cell numbers without the drawbacks of allografting or autografting.

However, reliable protocols capable of expanding the patient's cell sample in vitro to therapeutic numbers and producing tissue engineered grafts of sufficient functionality are yet to be developed. Mathematical modelling provides a complimentary tool to gain insight into and control of different factors in the tissue culture. It is a highly time and cost effective tool to simulate tissue culture outcomes under different operating conditions. Modelling can be used to propose protocols which promote the functionality of the engineered bone tissue and scale its production to clinically-relevant size.

Here we develop a mathematical model to simulate the behaviour of cells cultured in static conditions on bioactive glass microcarriers. The use of microcarriers is a suitable expansion strategy as it limits the need for passaging and preserves the cell phenotype by providing 3D cellular interaction.

The model is based on a set of coupled differential equations describing cell population dynamics and nutrient distribution. We use reaction-diffusion equations to model the transport of oxygen, glucose and lactic acid in the system. Metabolic consumption of glucose and oxygen is modelled by Michaelis-Menten kinetics equations and is coupled to lactic acid production. The cell species are modelled through a variation of the logistic growth law in which proliferation is linearly dependent on local oxygen concentration.

We successfully parameterise the model by data fitting to experimental data obtained by our group and define coefficients for the cell expansion potential of each microcarrier biomaterial used experimentally. We use this predictive model to inform future in vitro culture settings and identify more efficient combinations of biomaterials, cell seeding numbers and culture duration. Within the context of obtaining stem cells by bone marrow aspiration, we propose a material type capable of expanding the lowest seeding number.

The simulation results demonstrate that the model can be used to improve the culture protocol.