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A PARAMETERISED CELL-SOLUTE MODEL TO AID PERIPHERAL NERVE CONSTRUCT DESIGN

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Summary: Peripheral nerve injuries have a high global economic cost and are often debilitating for patients. The current gold-standard solution is to bridge the severed nerve ends with an autograft, but the supply of adequate tissue is limited and the procedure often results in comorbidities. Tissue engineered constructs are a promising alternative, but currently do not match the clinical outcomes of the autograft. So far, experimental studies have been used to refine the design of constructs, with varying degrees of success. Due to the multitude of variables involved in nerve repair, and the high costs associated with experimental work, mathematical and computational modelling has great potential for application in this field. Here we demonstrate this potential with a model to describe the interactions between the seeded cell density and oxygen and VEGF (vascular endothelial growth factor) concentrations in a collagen construct. Vascularisation and cell survival are vitally important for effective nerve repair, and this model will provide spatio-temporal estimates of variables crucial to controlling these processes within a nerve repair construct.

The model consists of a set of coupled partial differential equations to describe cell proliferation and death, VEGF diffusion, secretion and decay, and oxygen diffusion and consumption. In vitro data was collected to enable parameterisation of the model. Collagen gels with different initial seeded cell densities were incubated under different oxygen conditions, and measurements of VEGF concentration and cell density were taken after 24h. COMSOL Multiphysics finite element software was used to conduct parameterisation against the data using a 2D geometry representative of the experimental set up.

Parameters extracted based on the in vitro data are input into a model simulation in a cylindrical geometry representative of a nerve repair construct. Boundary (e.g. Neumann/Dirichlet) and initial conditions (e.g. seeded cell distribution) are varied to mimic the effect of different construct designs upon the distributions of the variables over time. The most promising designs based on cell survival are identified and prioritised for future in vivo testing. In combination with the traditional experimental approach, the model will help to streamline and accelerate the improvement of nerve repair construct designs.