A mathematical framework for nerve regeneration in implantable conduits

Conference or Workshop Item

P-88: A Mathematical Framework for Nerve Regeneration in Implantable Conduits

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INTRODUCTION:
Matching the performance of autografts with engineered scaffolds remains a challenge in peripheral nerve repair. A combination of 3D biomimetic architecture interspersed with 2D surfaces has been hypothesized to be an ideal environment for neurite regeneration[1]. However, the problem of how best to arrange material within a conduit is an open one[2]. Optimizing material parameters such as density, cross-sectional geometry and spatial distribution would require an extensive programme of experimental testing. By contrast, developing a modelling framework that is capable of testing key parameters may accelerate the design process, and reduce the dependency on animal testing.

METHODS:
A model was devised to simulate neuronal growth inside a cylindrical conduit. The trajectories of neurites are generated according to a 3D random walk process with a spatially dependent probability distribution. To mimic preferred neuronal growth on particular surfaces, a topographical bias is included. Parameters can be adjusted to mimic realistic dimensions and growth rates, as well as the rate of sprout formation at the proximal stump.

RESULTS:
The sensitivity of the hit ratio (proportion of neurites exceeding a prescribed longitudinal distance over a 2 week period) to changes in the porosity was investigated. Simulations were performed for a conduit featuring sheets of material. Fig. 1 shows the existence of an optimal porosity, representative of the competition between the total substrate available to aid growth and the obstruction of neurites at the entrance to the conduit.

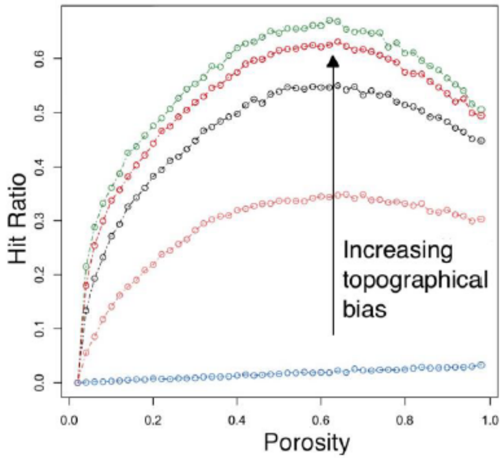

Fig. 1 Simulated hit ratios for different porosity values. Different curves correspond to varying topographical biases.

DISCUSSION & CONCLUSIONS:
We demonstrate the utility of a stochastic model for peripheral nerve regeneration and its ability to mimic experiments. The model presented predicts the existence of an optimal porosity value for one spatial arrangement of material, which could be adapted to investigate more complex designs.

More importantly, perhaps, is the promise indicated by this dual-approach, whereby wet & dry approaches can be built and updated simultaneously - experiments can verify and refine a model, and a model can help motivate experimental specifications and investigate novel biological hypotheses.

REFERENCES:
1. M. Bellamkonda (2006), *Biomaterials* **27**: 151-60.
2. M. Georgiou et al (2013), *Biomaterials* **34**: 7335-43.