

Mathematical Modelling in Tissue Engineering

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We believe that mathematical modelling has an important role to play in understanding and interpreting experimental data. We aim to outline below the process of mathematical modelling and illustrate the potential insights it may afford in medicine and in tissue engineering in particular.

Biological systems are inherently complex. The art of mathematical modelling is to unravel this complexity by identifying the key features of a given system. We do this by deriving equations based on fundamental principles such as conservation of mass and momentum, which govern its behaviour. Using various mathematical techniques and computer simulations, we can solve these equations over a wide range of physiological parameter values, thereby generating predictions which can be tested in the laboratory. The resulting insights can accelerate progress by suggesting the most fruitful lines of inquiry and thus reduce costs of experimental efforts. Furthermore, model predictions may also suggest new avenues for investigation.

A particularly productive field of mathematical medicine has been the study of solid tumour growth, [2] being a notable example. The aim of this study was to help resolve the debate in the literature on the mechanism of tumour encapsulation, there being two leading hypotheses: *active* (surrounding cells secrete collagen in an attempt to confine the tumour) and *passive* (tumour expansion compresses the surrounding extra-cellular matrix into a capsule). Using mathematical models, the authors found that the passive hypothesis provides the more natural explanation of encapsulation.

The field of tissue engineering presents numerous opportunities for mathematical modelling, in areas such as cell signalling and cell-substrate

interactions. For example, a recent study on cell signalling in engineered urothelium tissue showed that a proposed reaction pathway for cellular differentiation (in response to the drug Troglidazone) was inadequate to explain the experimental observations [3]. A new feedback mechanism, in which activation of the signalling pathway stimulated active transport of the drug across the cell membrane, was postulated. The new model appears to show better agreement with the behaviour observed in the laboratory; it now remains for experimental investigations to determine the mechanism that operates in practice.

Our particular focus is on optimising the formation, functionality and viability of liver-cell spheroids *in vitro*, by modelling the interplay of cell-cell and cell-matrix interactions. Preliminary results from a mathematical model of the early stages of spheroid formation appear to indicate that compliant substrates (those with small Young's modulus and viscosity) are preferential for aggregation, as they offer least resistance to the motion of the cells.

REFERENCES: ¹ J. Sherratt, 'Trust me, I'm a mathematician', *New Scientist*, 1995. ²T. L. Jackson and H. M. Byrne *Mathematical Biosciences*, 180, 307-328, 2002. ³ P. Woodroffe, J. Keener, O. Jensen, A. Hazel and A. Jones, 'Cell Signalling in the Urothelium', Proceedings of the Third Mathematics in Medicine Conference, p37-47, 2002 (available online).

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