

Bioreactor design and use in regenerative medicine the benefit of mathematical modelling

Bioreactors have been used in regenerative medicine research for several decades. Although clinical success has been limited to a few headline-grabbing stories in that time, it remains an active field of research and progress continues to be made.

Bioreactor systems come in all shapes and sizes: some models are borrowed from various industrial applications, whereas others have been developed with a specific tissue or cell type in mind. Common to all is the need to understand the complex interaction between the growing cells and their external environment provided by the bioreactor. This is essential in order for promising results in the laboratory to be reproducible and, eventually, translated and scaled up to a clinical setting. As well as growing functional, replacement tissue for implantation into the human body, tissue engineered substitutes can have important applications in areas such as drug toxicity testing, aiming to reduce the occurrence of drug attrition.

[Deciding what the focus of a model should be is a skill in itself, and care should be taken to ensure the approach is suitable and tailored to the specific application.](#)

In part due to the inherent complexity of biological systems, barriers to success in this field include the cost and duration of experiments, the problem of scale-up (for instance growing and maintaining a viable blood



supply to larger tissue constructs), and the individuality of different cell types and their particular requirements for growth and survival.

Taking note of these challenges, mathematical and computational modelling of bioreactors and tissue growth is becoming more widespread as a way of complementing ongoing experimental research¹. This can take a variety of forms, for instance focussing on the macroscale setup of the whole bioreactor and tissue construct, or on individual cells at a microscale level.

Clearly, simplifications must be made when developing a theoretical model of such systems, as it would be unfeasible (if not impossible) to do otherwise. Deciding what the focus of a model should be is a skill in itself, and care should be taken to ensure the approach is suitable and tailored to the specific application. For instance, it may be particularly important to understand the fluid flow through a bioreactor in order to calculate the stresses and strains on a tissue at different times and locations within the system.

In a different setup, it may be more useful to model the

transport and subsequent distribution of limiting nutrients, growth factors or waste products. If desirable, this can in turn be coupled to a description of the cells or tissue via (for example) their growth, motility or differentiation. Mathematical models of such features need not be overly complicated but can be of great use in informing future experimental design and determining more favourable operating conditions. In addition, theoretical results can be found for a variety of parameters, enabling key trends to be identified without the need to carry out several independent experiments.

As a result, significant time and cost savings can be made, and experimental results can be supported by an enhanced understanding of the underlying physical processes at play, leading to a more robust and efficient research programme.

[Natalie Hearmon,](#)
[Sagentia](#)

¹Continuum modelling of in vitro tissue engineering: a review. O'Dea, R.D., Byrne, H.M. and Waters, S.L. Springer, 2013.