Realtime permeability estimation during tissue growth within different scaffold designs

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Abstract.
Having an accurate estimation for permeability for scaffolds during tissue growth is highly desirable by tissue engineers. Furthermore, scaffold with different topologies will result in different tissue growth kinetics and different permeabilities. In this study, we aim to reveal how a scaffolds permeability changes with neo-tissue growth within different scaffold architectures. To achieve this, different analytical permeability calculations will be compared, then the most suitable one will be applied to an in silico neo-tissue growth model, for 5 distinct TPMS architectures. The outcome is anticipated to guide the scaffold design and real-time optimisation of bioreactor loading for in vitro tissue engineering / organoid applications.

Introduction

Determinable permeability is valued by tissue engineers who design and manufacture tissue engineering scaffolds as permeability is important for nutrient transport through porous scaffolds and influencing internal micro-mechanical environment, which can influence internal tissue formation kinetics [1]. Therefore, it is important to have an accurate and complete understanding of how permeability is affected by the topology of scaffold struts. Triply periodic minimal surfaces (TPMS) are emerging promising scaffold structures in the tissue engineering field [1]. Previous studies have used regression analysis to relate permeability to geometrical characteristics; however, a comprehensive understanding of how the complex features of TPMS structures and internal neo-tissue formation will influence overall permeability is still lacking. In this study, to reveal the scaffolds permeability change with neo-tissue growth, first, different existing analytical methods of porous media permeability calculation were assessed. Then the most suitable one was applied to calculate the permeability of tissue-infilled scaffold. The tissue-filling within scaffolds was simulated with the in silico tissue growth model developed by Egan et al. [2]. Five different TPMS topologies with different porosities and pore sizes were investigated in this study. The outcome is anticipated to guide the scaffold design and real-time optimisation of bioreactor loading for in vitro application.

Methods

The TPMS structures were generated in 2 forms (voxel and isosurface) within MATLAB and the specific surface area, tortuosity, porosity, pore size, throat size, fibre radius were recorded for each scaffold. The specific surface area (S_{SA}) was determined for the isosurface form whilst the other parameters were determined in voxel form. The isosurface representations were inverted and the permeability of scaffolds were calculated based on Darcy's law, where the pressure drop was obtained by computational fluid dynamics (CFD) approach. The permeability from CFD model was compared to different analytical models of permeability calculation. The most accurate one was chosen for real-time permeability calculation during neo-tissue growth within scaffolds. In the tissue growth model that was previously developed by Egan et al. [2], the neo-tissue grows appositionally on the struts with the growth rate governed by local voxel curvature.

Results

Figure 1 shows a percentage different comparing permeability from the CFD simulations to values of permeability obtained from several permeability models. The Berg permeability model [3] produces the second lowest mean percentage difference and does not require different constant values for each topology so was chosen as the model for predicting permeability during neo-tissue growth.

Figure 2 indicates the results for the neo-tissue growth part of the study, where the initial permeability of the CFD models is graphed against the mean void filling rate. The number of time steps to complete the total neo-tissue growth was shown in [2] to correlate with permeability. Figure 2 indicates that lower permeabilities will result in a higher mean void filling rate, which means that total neo-tissue growth will occur faster, this trend is corroborated in [2]. The results also indicate that topology is a factor in whether cell growth will complete, where the diamond topology had a higher rate of non-completion.

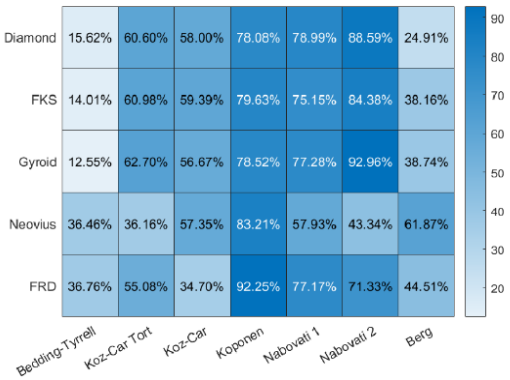

Figure 1: Percentage difference map for the different permeability equation for TPMS geometries.

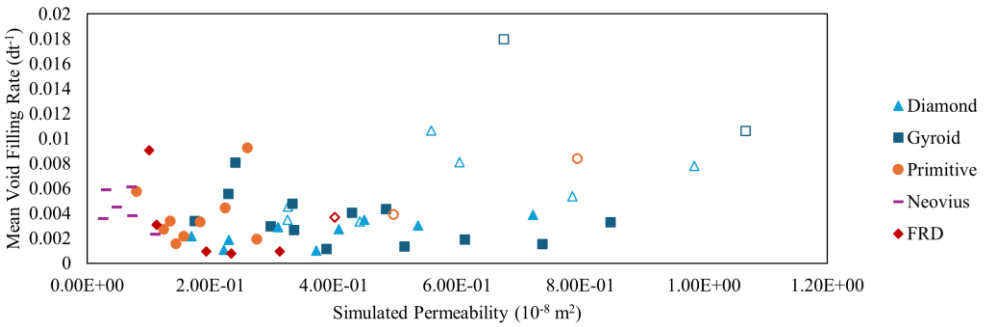

Figure 2: Mean void filling rate compared to the simulated permeability for different TPMS types

Discussion & Conclusion

In this study, permeability was calculated for 5 different TPMS topologies, each with a range of porosities and pore sizes. Additionally, neo-tissue growth within those scaffolds was simulated, and it was found that for similar permeability TPMS structures have lower void filling rates than beam-based structures and the trade-off between permeability and void filling rate is less critical for TPMS structures. This neo-tissue growth model was then integrated with one of the permeability equations so real-time permeability can be determined with neo-tissue growth. As an application case study, using a semi-empirical relationship, which relates permeability to WSS, this novel method will allow researchers to achieve real-time optimisation of bioreactor loading conditions to control the WSS on cells. For example, in Figure 3, it was found that the permeability changes as neo-tissue grows on the scaffold. If in a perfusion bioreactor environment, wall shear stress (WSS) is also found for each time step using an empirical relationship between permeability and WSS [4]. Using these relationships will allow researchers to achieve real-time optimisation of the bioreactor loading to control the WSS on cells.

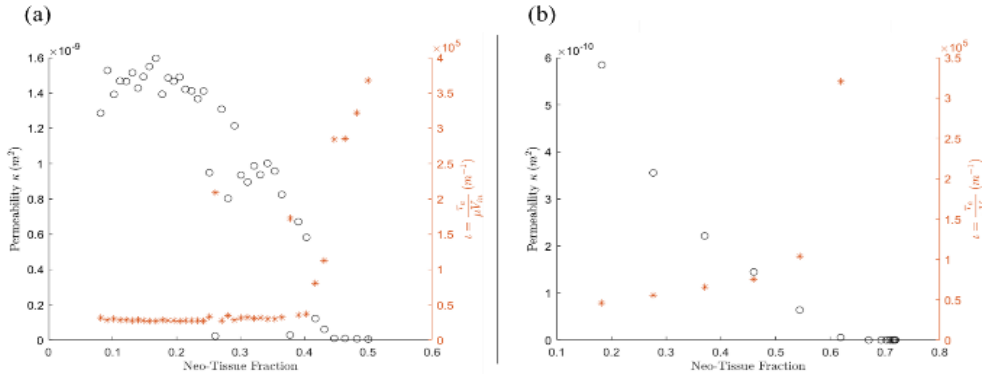

Figure 3: (a) Neovius geometry and (b) gyroid geometry fluid properties due to neo-tissue growth

References

[1] J. Zhang, et al. Mater. & Des. Vol 218 (2022): 110665.
[2] Egan P.F., et al. Biomech. Model. Mechanobiol. Vol 17 (2018): 1481–1495.
[3] Berg C.F., Transp Porous Med. Vol 103 (2014): 381–400.
[4] M. Bedding-Tyrrell, et al. J. Eng. Des. Vol 36 (2025): 1631-1645.