How maths can help grow tissues

The tissues in our bodies are in a dynamic environment due to the movement of our limbs and the flow of blood. This motion helps cells to grow as it stimulates them mechanically and also provides a continuous supply of nutrients. To grow tissues in the lab for substituting damaged organs or for drug testing, we need to provide the same stimuli to cells in three dimensional (3D) scaffolds so as to recreate the same environment as in the body. Scientists have developed bioreactors which pump or agitate nutrients to do this, but it is difficult to ensure that cells in the middle of the scaffold receive adequate oxygen and other chemical and mechanical signals. In this study, we developed a multiscale model to determine the level of oxygen, pressure and fluid induced forces in the center of a porous scaffold inside a bioreactor. The modeling method is called computational fluid dynamics using finite element methods. Basically, our bioreactor and scaffold are divided into tiny elements, either in 2D triangles or 3D tetrahedrons (Fig. 1) and the speed of a fluid particle or concentration of nutrient is calculated for each element and then summed vectorially for all elements put together.

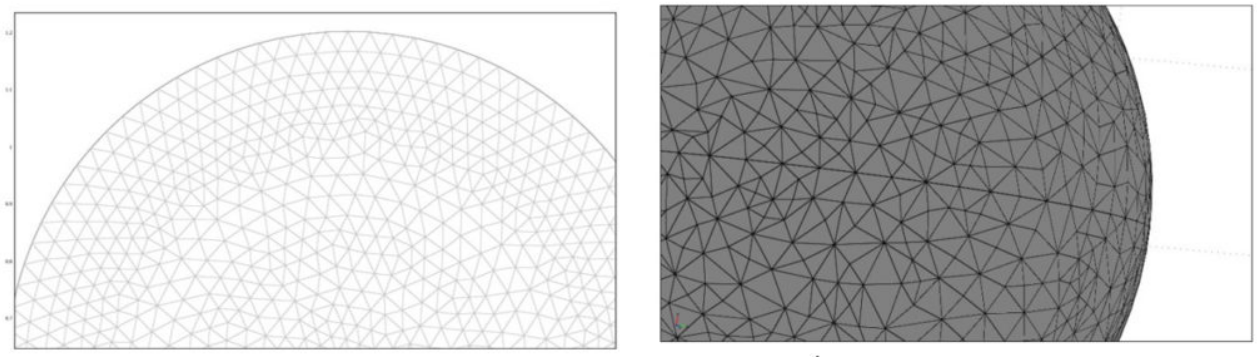

Fig. 1. 2 and 3D finite element representations of a sphere

The bioreactor is called a Squeeze Pressure (SQPR) bioreactor. Nutrients move around in the SQPR thanks to a piston which sloshes the fluid around and in the scaffold by moving up and down close to, but not touching, it. The moving fluid brings nutrients with it and it also generates forces such as pressure and shear. Because the moving fluid interacts with the scaffold in a complicated, but cyclic manner, we broke down the problem of determining forces and nutrients (oxygen is the main one because that is where cell metabolism starts) into separate units, each at a different scale starting from centimetres, to millimetres to microns and used the solution of each problem as the input to a new different, smaller scale unit. The method used is shown in Figure 2.

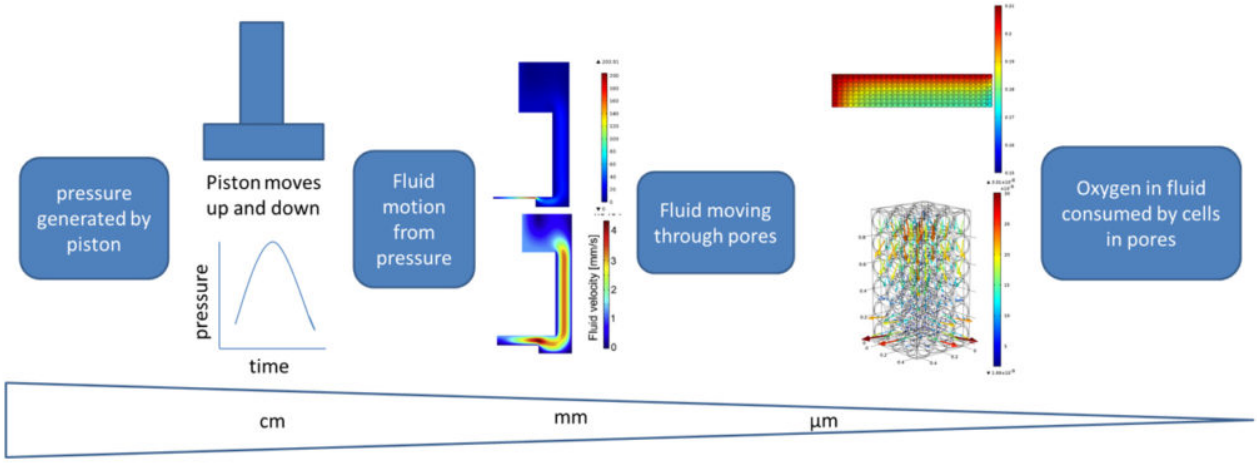

Fig. 2. The multiscale modeling approach used, illustrating how the cyclic pressure generated by the SQPR bioreactor piston can be used to model microscale cell oxygen consumption in a 3D porous matrix.

We show that cells have sufficient oxygen to survive in the bioreactor because the moving piston continually replaces the oxygen that is consumed. This was confirmed experimentally by seeding heart stem cells on a scaffold in the SQPR. With respect to 2D, the 3D models give results that are much closer to what we observe experimentally. The approach can be used to predict how cells behave in complex 3D environments and help in the design of more efficient cell culture systems for tissue growth and regeneration.

Arti Ahluwalia, Federica Boschetti, Marco Ferroni
University of Pisa and Polytechnic of Milan, Italy

Publication

Modeling the fluid-dynamics and oxygen consumption in a porous scaffold stimulated by cyclic squeeze pressure.
Ferroni M, Giusti S, Nascimento D, Silva A, Boschetti F, Ahluwalia A
Med Eng Phys. 2016 Aug