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Oxygen distribution in the liver lobule: Three dimensional computational Models

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Content

We develop a computational model for the transport and metabolism of drugs as well as oxygen in the functional unit of the liver called the lobule. The functional unit of an organ is the smallest structural unit that can independently serve all of the organ's functions.
In previous studies, starting from a simple idealized model of the lobule composed of liver cells and sinusoid flow paths, we discussed the effects of structural variation and inhomogeneity on the sinusoids flow properties and related this to random distributions, and fractal and percolation concepts. As well, possible effects of metabolic zonation of liver cells on drug concentration levels inside the lobule were considered. Zonation has been attributed primarily to non-uniform distribution of oxygen across the lobule, with the periportal zone experiencing relatively high concentrations of oxygen while the perivenal zones see near hypoxic levels of oxygen.
Here, we apply our model to track oxygen distribution and metabolism across the lobule. Since oxygen is small molecule, molecular diffusion can be expected to play a dominant role. Furthermore, to capture more realistic structures, we introduce 3D hexagonal based models with one input (arterial blood flow from the portal vein) and six outputs (hepatic veins) to represent a typical liver lobule. We also implement a novel sequential diffusion-limited aggregation (DLA) method in constructing the sinusoidal network in the lobule to mimic their realistic structural variation. With this approach, we are able to analyze predicted drug concentration levels observed exiting the lobule and relate this with their detailed distribution inside the lobule, and compare the results with our earlier idealized lobule models.
The convective-diffusive-reactive problem was solved and the resulting steady state flow of oxygen on this 3D structure is furthermore used to predict the oxygen-generated enzyme distributions in liver cells responsible for lobule zonation.
Such analysis indicates the variability of response which can be expected from individual lobule sections in healthy livers due to modified convective structures in this well-vascularized tissue. Since various liver diseases can be thought to produce structural variations in the lobule, our analysis also gives insight into the role of disease on liver function and performance.

Primary author(s) : REZANIA, Vahid (MacEwan University)

Co-author(s) : Dr. COOMBE, Dennis (Computer Modelling Group, Ltd.); Dr. TUSZYNSKI, Jack (University of Alberta)

Presenter(s) : REZANIA, Vahid (MacEwan University)

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