Towards a full digital liver twin of drug-induced damage, regeneration and disease progression

Jieling Zhao

Digital twin is the projection of the real world object to the digital world. It has been widely used to study the biological and medical phenomena such as to understand the biomechanical growth control mechanisms of liver regeneration and to explore the extrapolation strategies for drug-induced liver injury. In this talk, we present a digital twin of the liver and its application to drug-induced liver damage, liver regeneration and fibrosis formation as a prominent example of a disease process. This digital twin is based on a biophysics-based computational model which can accurately capture the deformation of cells, capillaries, and extracellular matrix according to their biomechanical properties. As drug-induced damage overdosing paracetamol (acetaminophen) is studied in a multilevel model integrating drug detoxification in each individual hepatocytes according to the processes in the respective liver zones (zonatation). The regeneration process triggered by the drug is based on a complex cross-talk between cells exchanging extracellular signals. This intercellular signaling network is integrated into the digital twin to allow the communication between various cell types through corresponding signals. We show that for the application of liver regeneration, the digital twin could help identify a set of successful alternative mechanisms controversly discussed in the biological and medical community for a perfect liver recovery and predict the effect of depletion certain cell types. Repetitive damage has been shown to cause fibrosis characterized by deposition of extracellular matrix but the mechanism leading to the characteristic spatial pattern of fibrosis are not understood. The digital twin proposes a mechanism of how the fibrotic pattern is formed. In summary, here we show the potential of the digital twin for studying complex biological/medical problems at subcellular level and its role as a pillar complementary to real-world experiments in future.