Vivi Rottschafer (Mathematical Institute, University of Leiden)

Towards a 3D distribution model of drugs in the brain

Abstract

Development of drugs with adequate action on the brain is highly challenging. Quantitative understanding is needed on the highly complex processes that govern the concentration-profile of a drug, such as transport of the drug from blood to brain and subsequent distribution to the target site.

Existing models for prediction of drug distribution and effect consist of systems of ordinary differential equations to describe the pharmacokinetics of drugs in multiple physiological brain compartments. However, it is important to also take into account local brain distribution, as target expression in the brain can substantially differ between different regions in the brain.

On the way towards a 3D spatial drug distribution model of the brain, we first developed a 2D model that gives more detailed insight into the change of drug concentration in the brain in both time and space. The model consists of a system of a partial differential equation and ordinary differential equations that describe the concentration of free drug in the brain and the concentrations of free and bound receptors on the surface of the brain cells. In this model we integrate both the drug distribution and target interaction kinetics, to ultimately improve the prediction of drug action in the brain.