Samantha Sun

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Article 3

This paper proposes a two-compartmental model for a system that includes flow of analyte and the binding of the analyte to an immobilized receptor. Measurement of binding rate constants and kinetics is crucial in understanding the system and making future predictions, but there are several limitations to current methods of determining rate constants, which were highlighted in the introduction of this paper. Here, the authors propose a two-compartmental model, and test the model using computer-generated transport data.

1. Advantages of two-compartment ODE over a PDE model?

The authors decided to create a two-compartmental ODE model over a PDE model, which was used for their initial computer model of the system. The first advantage of using a simpler model is that it is simpler and does not require as much computational power or complex design to perform the analysis. Additionally, it’s a good idea to start with a simpler model, since it may be already able to answer the questions they needed to model to do, and if it doesn’t then the model can be added to. In this case, all the authors wanted was to calculate the concentration of the bound analyte, which may not require using a PDE system that considers analyte position or concentration gradient.

1. Level of certainty of conclusions based on verification + validation presented in paper?

The conclusions that were presented in the paper were (1) successful modeling of receptor-analyte binding concentration using their two-compartment model, (2) using this model to determine the rate constants and diffusion coefficient. For verification, the authors noted that their equation for the computer flow model matched with an already existing model for a BIACORE flow cell. For validation of the computer flow model, the authors ran simulations and confirmed that the behavior of their model is as expected. From there, they focused on their two-compartmental model. For verification, they again noted that their final model was identical to the effective rate constant model. They also checked their units. For validation, they implemented their computer model and measured the concentration of binding with their two-compartment model and a rapid mixing model (one that had been used in previous research), and they compared the model results with each other. Figure 9 demonstrates the best visual comparison, where it’s clear that the rapid mixing fits relatively well with the real concentrations, while the two-compartment model is essentially identical to the real data. This validation is essentially the “experiment” that the researchers run, and even after introducing noise to the system, the two-compartmental model performs well. With multiple steps of verification and validation, I have a high level of certainty for the conclusions of the paper.