

Assignment 3

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Week 3: Comparing simulation data with experimental data for two dosis

Assignment 1

We have to compare the data from the experiment with the simulation data, to assess the model validity. The best way to do this is plotting the model results and the experimental results in one graph. The model results have one value per time unit, the experimental results have multiple values per time unit. Either plot all data points of the experimental data using a scatterplot or calculate the median results for each time unit and plot a line of these median points.

[1] *Why is it best practice to plot the median for the experimental data?*

The median represents that middle value, cutting the set of values in half — 50% of the data values fall below and 50% lie above the median. No matter the shape of the distribution, the median is the measure of central tendency reflecting the middle position of the data values.

[2] *How do the results of the simulations depend on the dose and concentration of the drug?*

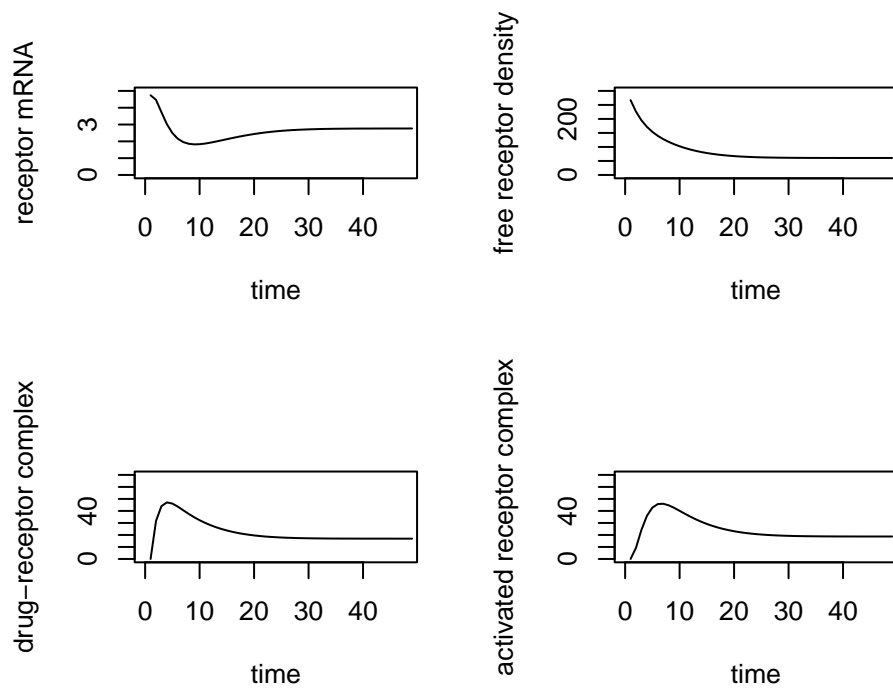


Figure 1: The normal receptor model

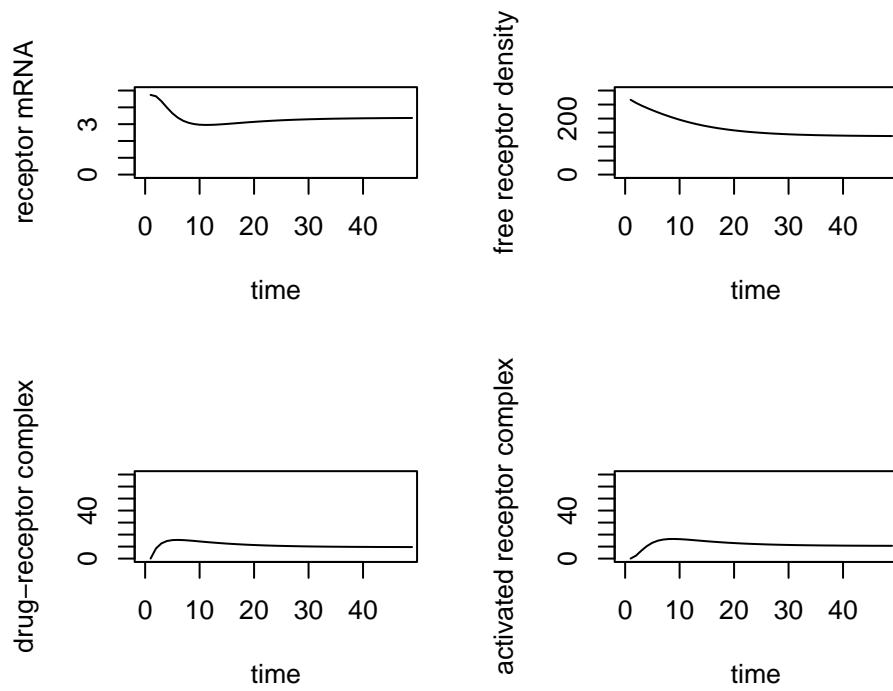


Figure 2: The receptor model with a lower D value

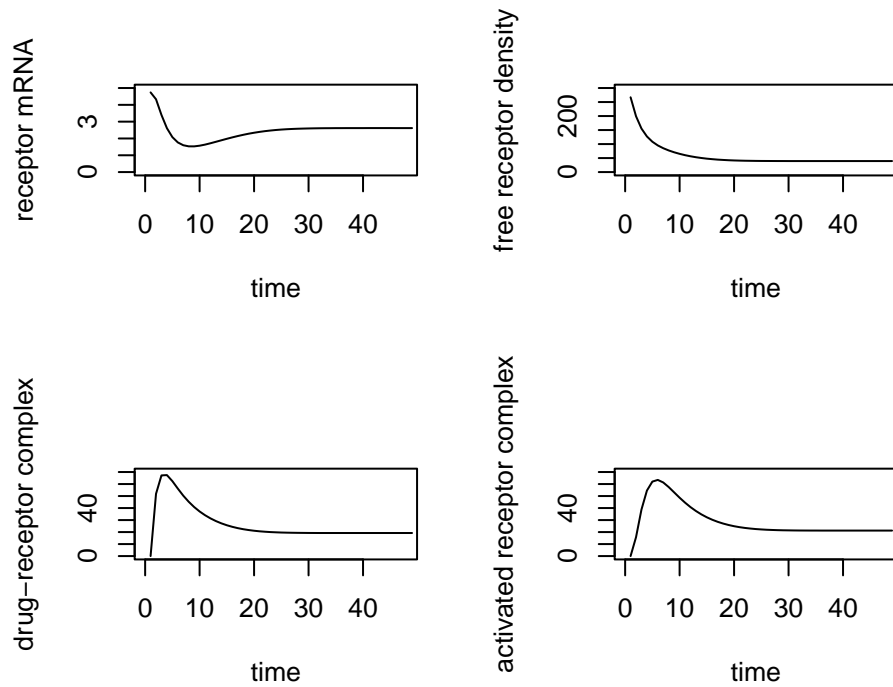


Figure 3: The receptor model with a higher D value

As you can see if you lower the D value, the amount of mRNA receptor and free receptor density gets higher than with a value of 20. But drug-receptor complex and activated drug complex goes down. If you up the value of D then the amount of mRNA receptor get slightly lower, the free receptor density is lower than before. Drug-receptor complex and activated drug complex have a higher peak than before and has a slightly higher equity.

[3] Are the results of the model in line with experimental data? If not, what could be the reason?

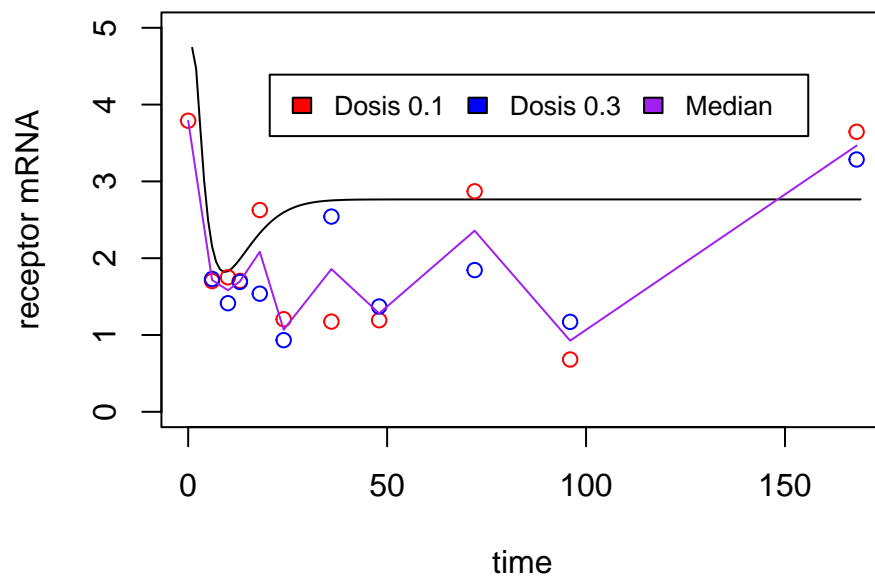


Figure 4: Receptor mRNA model with the data of the experiment

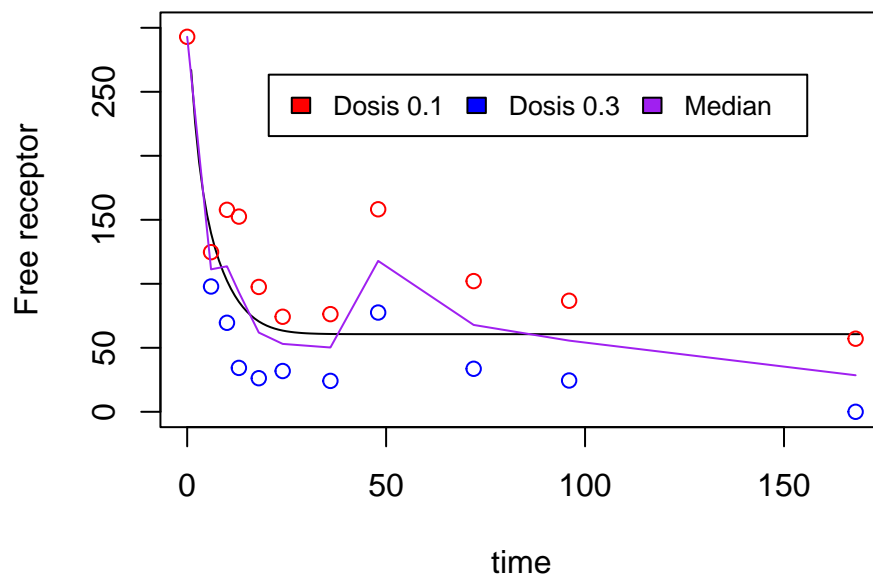
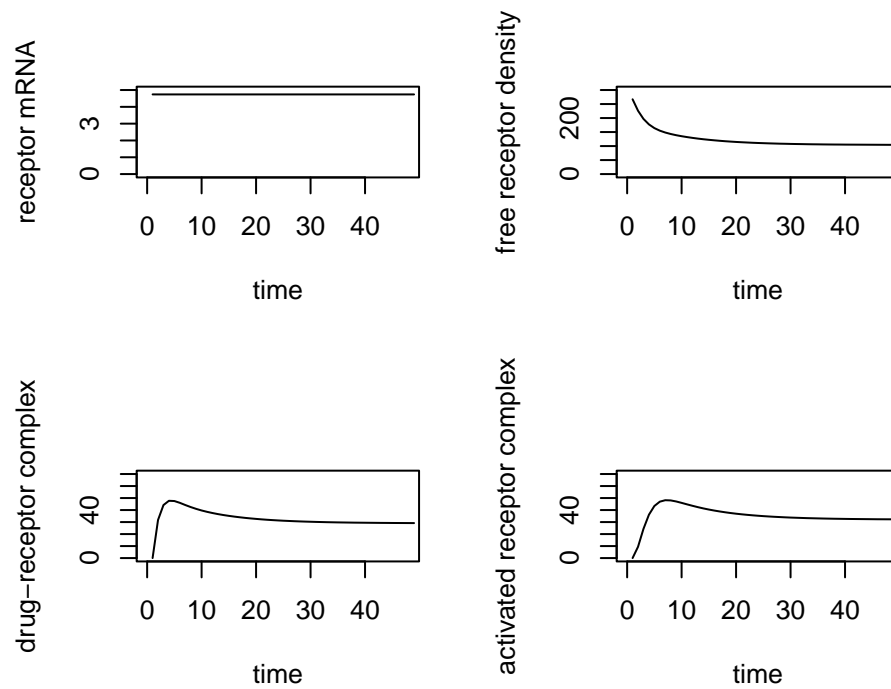


Figure 5: Receptor mRNA model with the data of the experiment

The free receptor model follows the data of the experiment. But the concentration of receptor mRNA doesn't follow the experimental data. A reason that is possible is that the data is skewed.

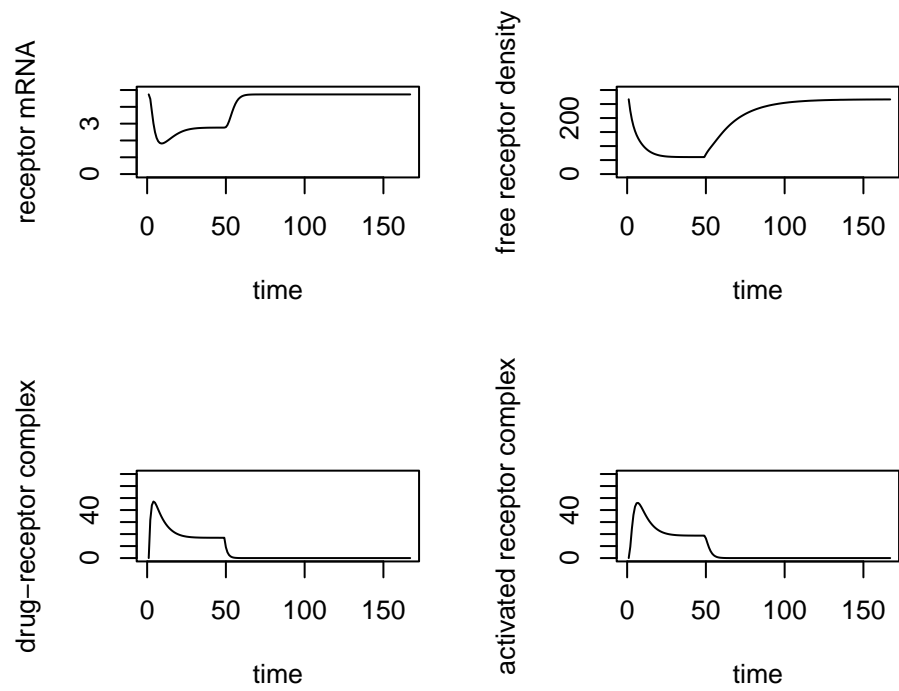
Assignment 2

[1] *What would be the time course concentration of the activated drug-receptor complex if there was no auto-regulation of glucocorticoid receptor, i.e. if there was not effect of drug on the synthesis of the receptor mRNA?*



The concentration of receptor mRNA doesn't change. As drug-receptor complex and activated receptor complex gets higher, the decrease of free receptor density slows down to a steady state.

[2] *What is the time course of receptor and mRNA concentrations when the drug treatment is stopped?*



The concentration of receptor mRNA doesn't change. As drug-receptor complex and activated receptor complex gets higher, the decrease of free receptor density slows down to a steady state.

[3]

What is the effect of different values of k_{on} and k_{re} on the receptor and mRNA dynamics?

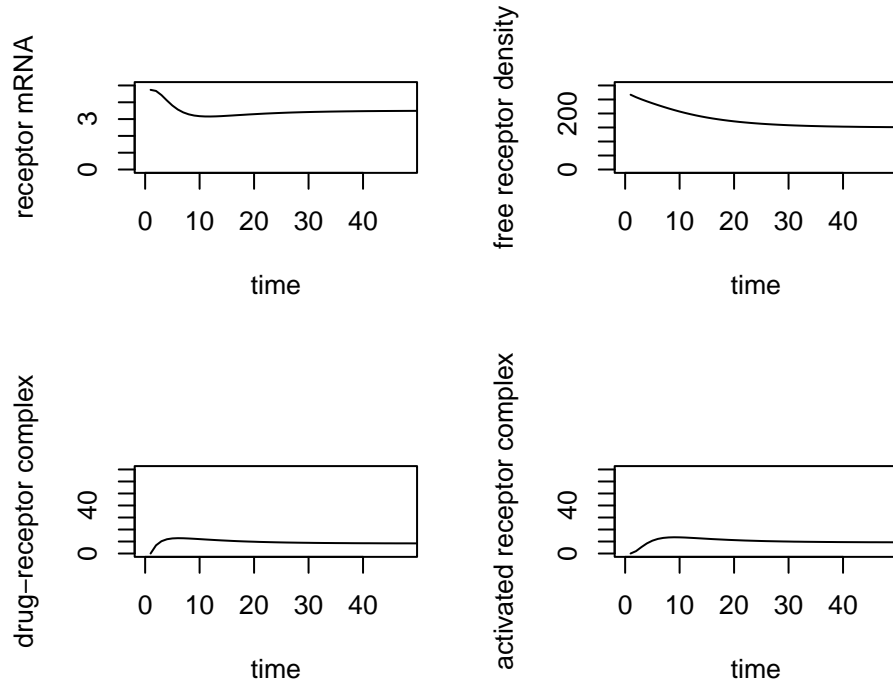


Figure 6: The receptor model and the effect of a decreased 5 fold value change of K_{on}

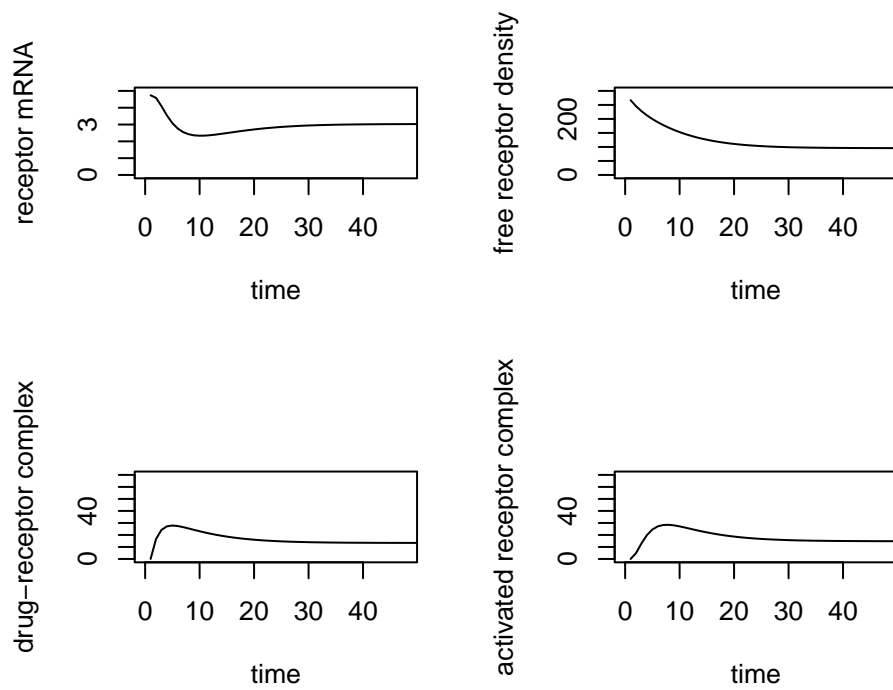


Figure 7: The receptor model and the effect of a decreased 2 fold value change of K_{on}

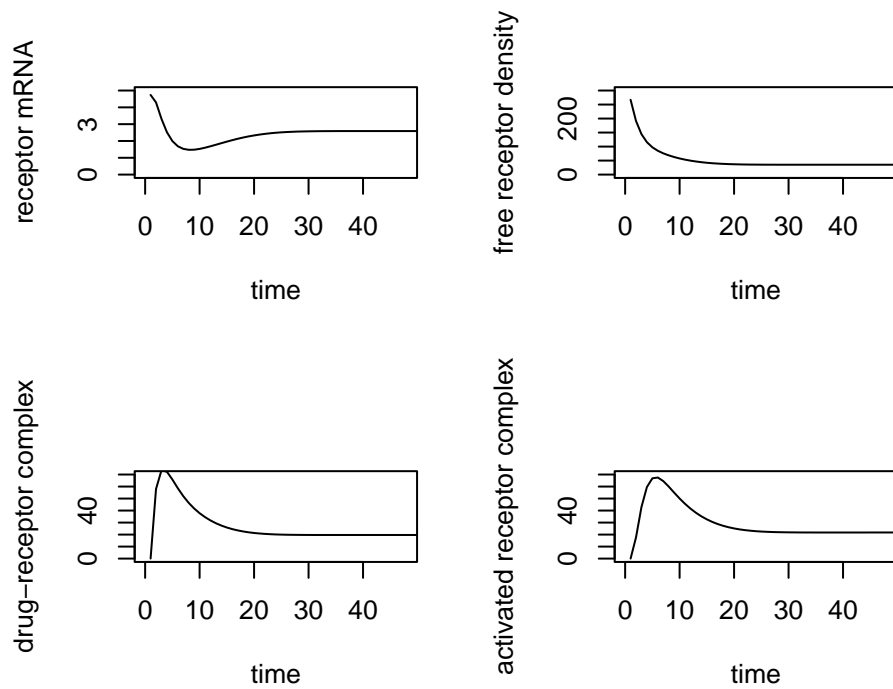


Figure 8: The receptor model and the effect of a increased 2 fold value change of K_{on}

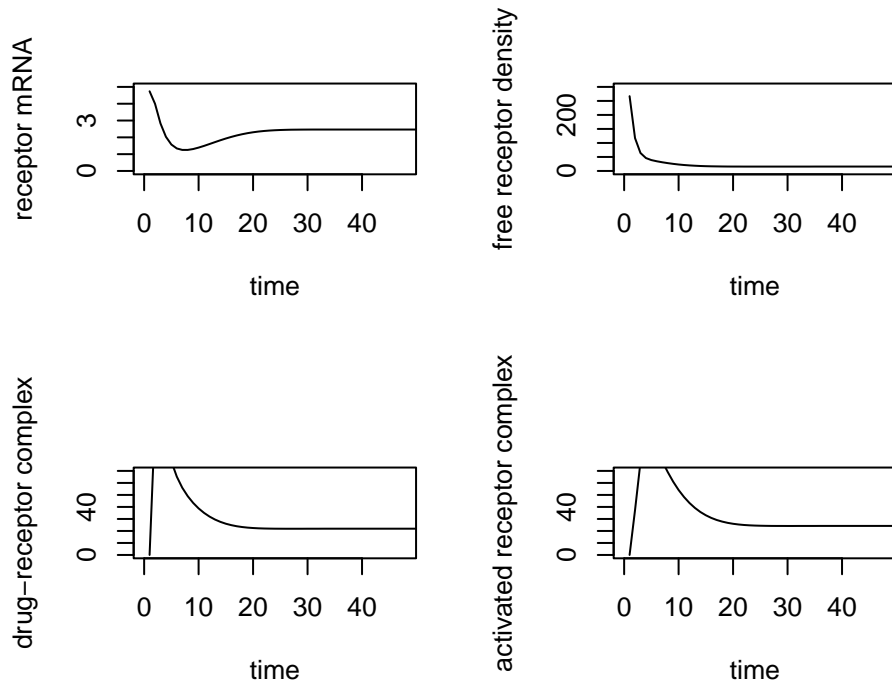


Figure 9: The receptor model and the effect of a increased 5 fold value change of K_{on}

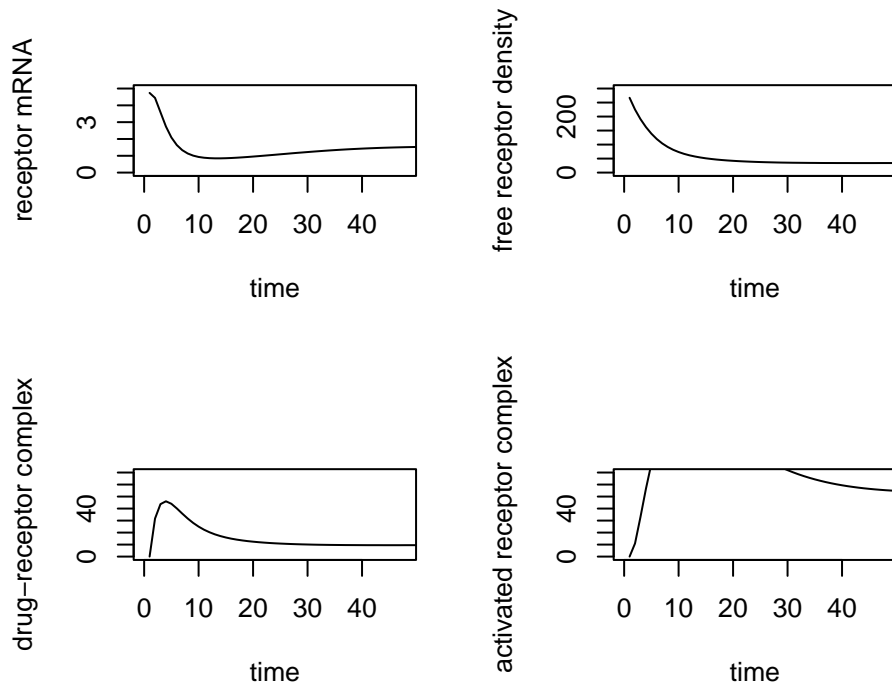


Figure 10: The receptor model and the effect of a decreased 5 fold value change of K_{re}

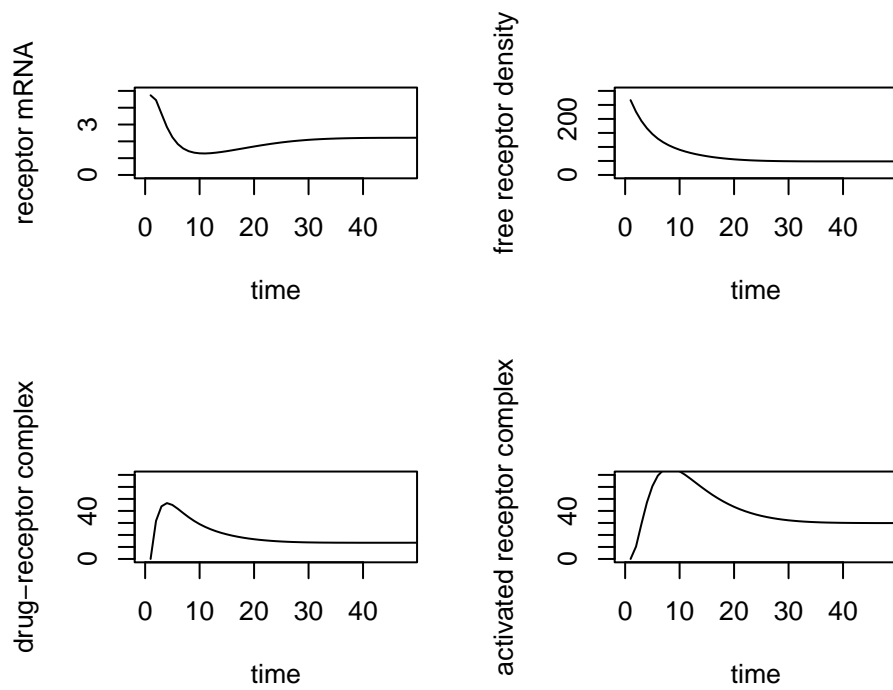


Figure 11: The receptor model and the effect of a decreased 2 fold value change of Kre

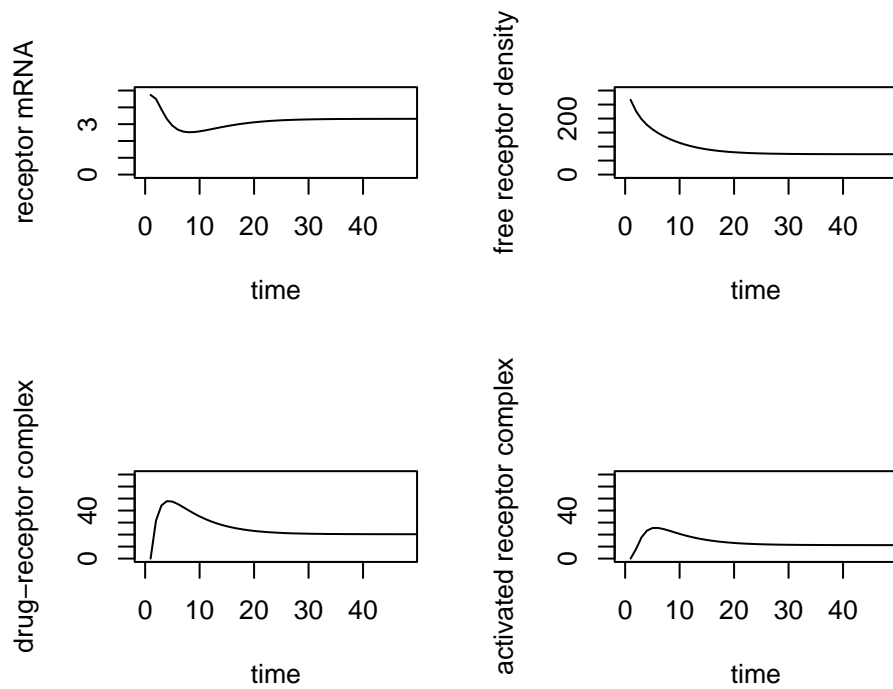


Figure 12: The receptor model and the effect of an increased 2 fold value change of Kre

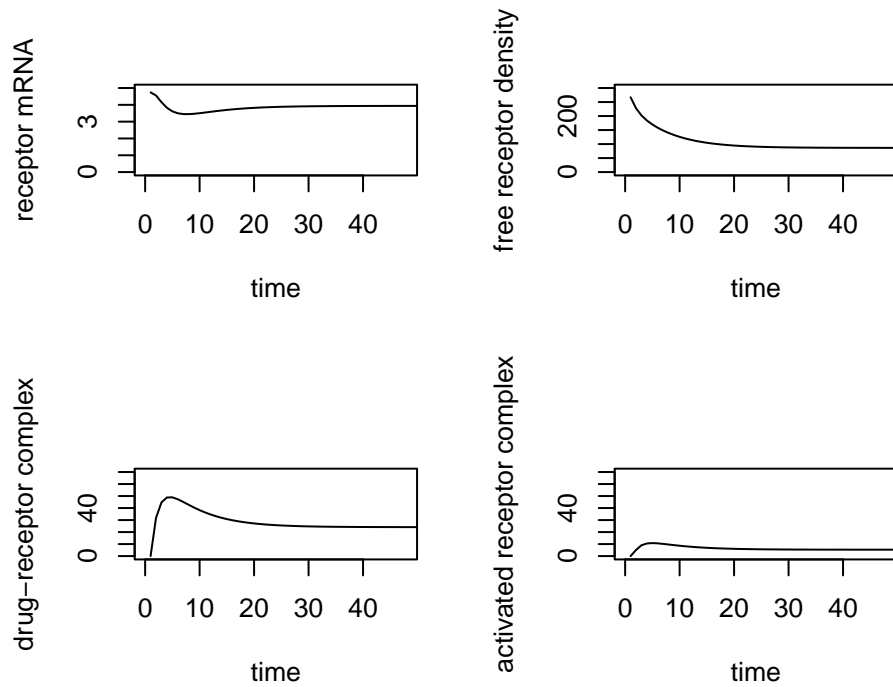


Figure 13: The receptor model and the effect of a increased 5 fold value change of Kre

If K_{on} is increased than you have a higher concentration drug-receptor complex and activated receptor complex and vice versa. If K_{re} is increased than you have a lower concentration drug-receptor complex and activated receptor and vice versa.

[4] *What would happen if the synthesis of the receptor was completely blocked?*

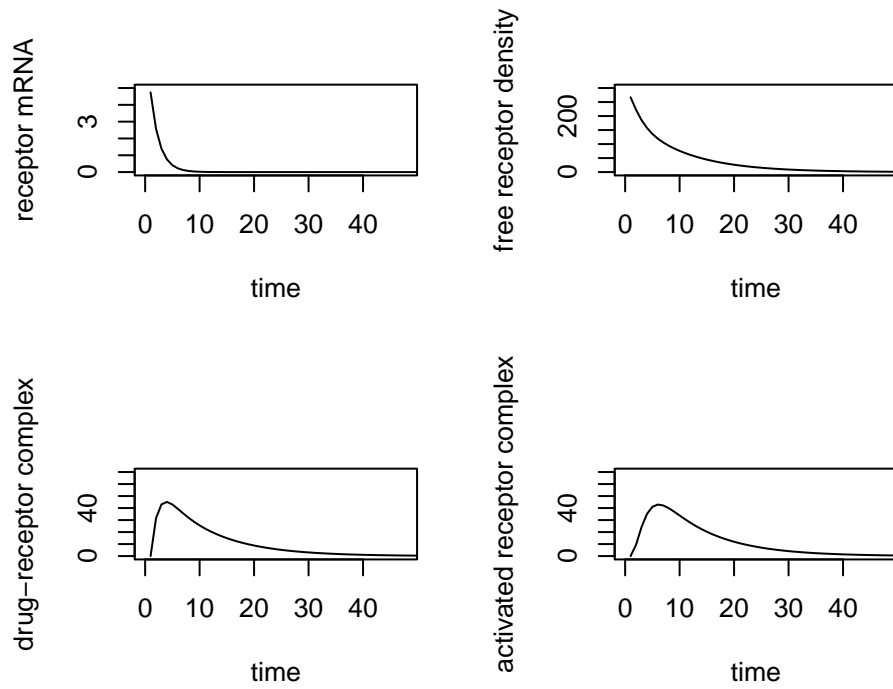


Figure 14: The receptor model if the synthesis of the receptor was completely blocked

The concentration of receptor mRNA steadily goes down to almost 0. Drug-receptor complex and activated receptor complex gets higher, until there isn't enough free receptor density.

[5]

What is the dynamic of the system when the baseline rate of production of mRNA of the receptor is increased or decreased 2 or 5 fold?

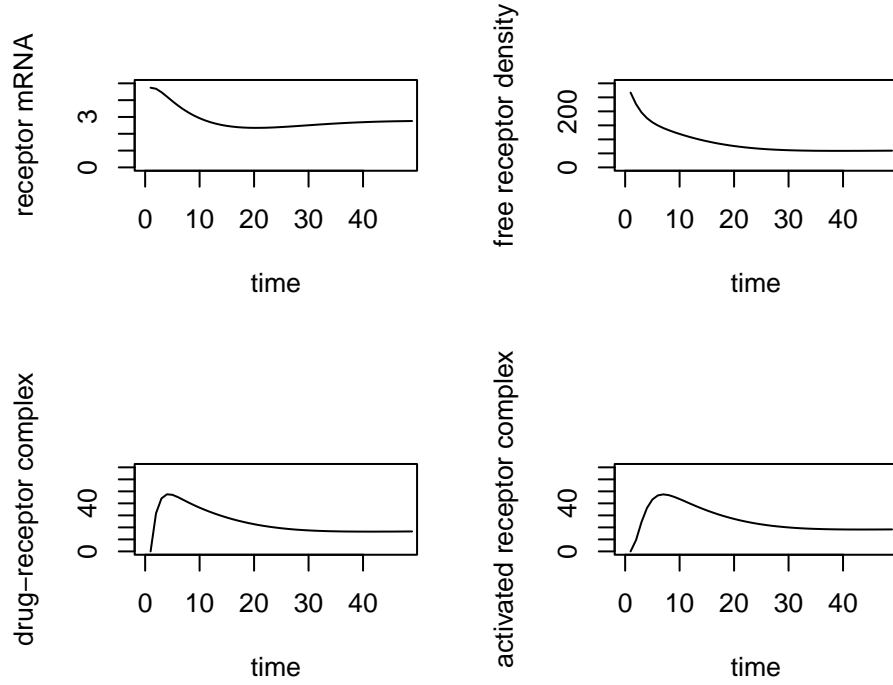


Figure 15: The receptor model if the baseline rate of production of mRNA of the receptor is decreased 5 fold

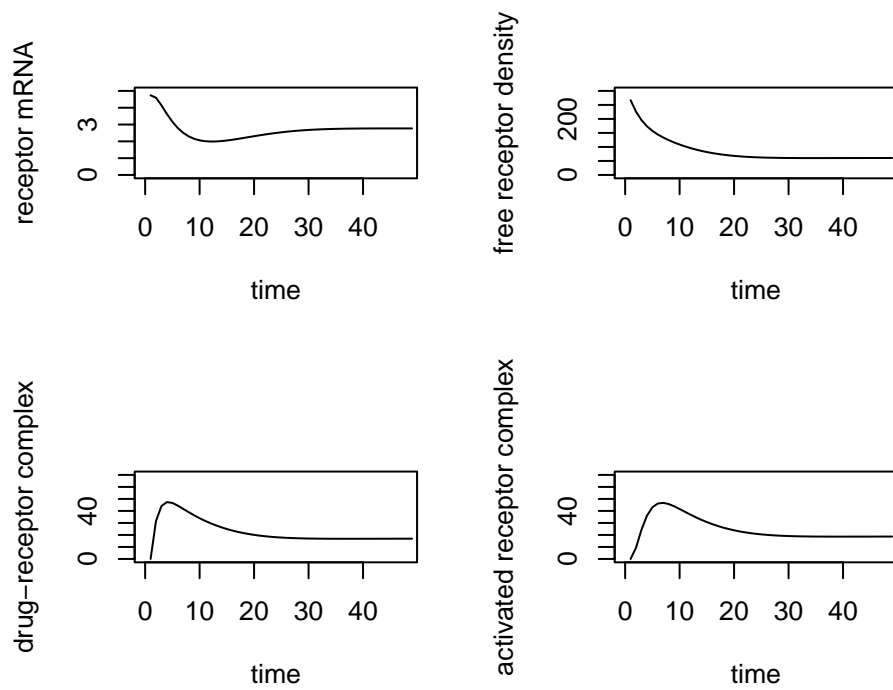


Figure 16: The receptor model if the baseline rate of production of mRNA of the receptor is decreased 2 fold

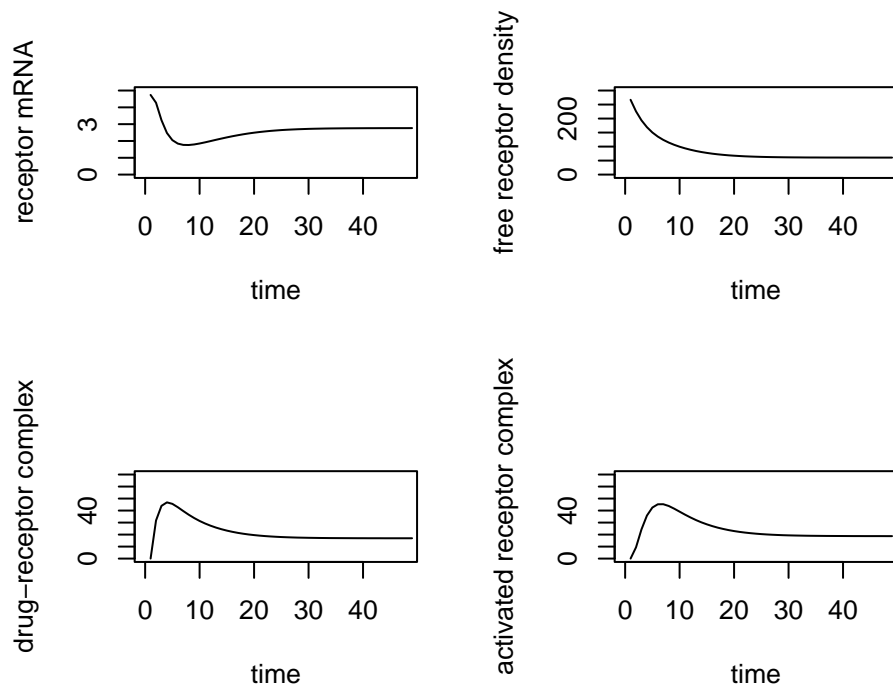


Figure 17: The receptor model if the baseline rate of production of mRNA of the receptor is increased 2 fold

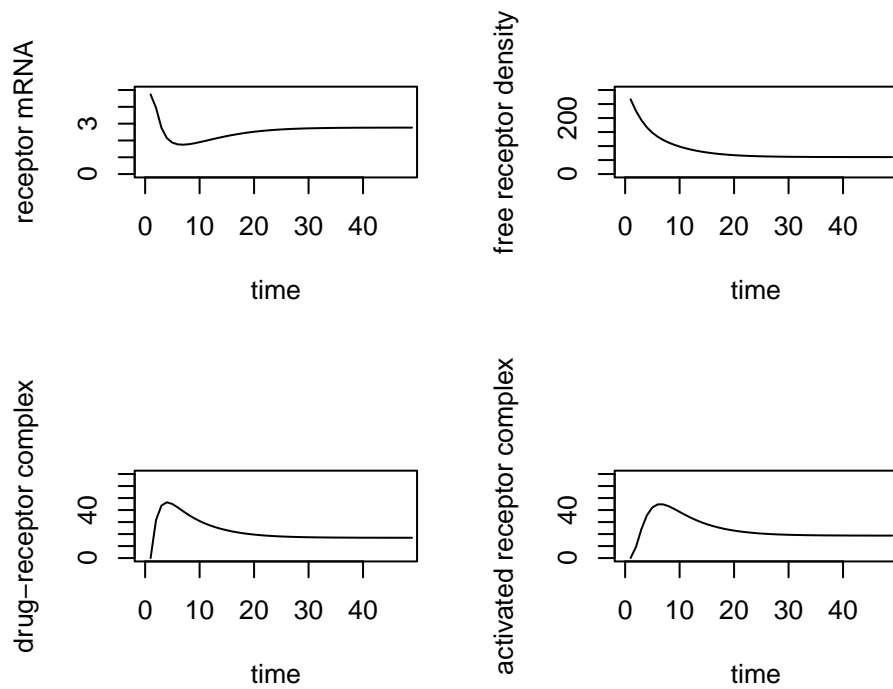


Figure 18: The receptor model if the baseline rate of production of mRNA of the receptor is increased 5 fold

Almost nothing changed than before. Nothing significant changed than before the increased/decreased 2/5 fold change.