SENSITIVITY ANALYSIS GLUCOCORTICOID SENSOR MODEL

In order to see which of the parameters were the most relevant for the model we performed a sensitivity analysis. For this, we took the values found in the literature and evaluated the model in a range that varied from one order of magnitude below the known value to one order of magnitude greater. Depending on how much the response varied we performed analysis in wider or closer ranges.

1. α_R: ***Basal production rate of the receptor (nmol/min):*** Looking at Graph 1 and Graph 2 we can see that there is a proportional relation between the basal production rate of the receptor and the system response. If the promoter of the chimera is stronger then the response of the system is going to be higher.

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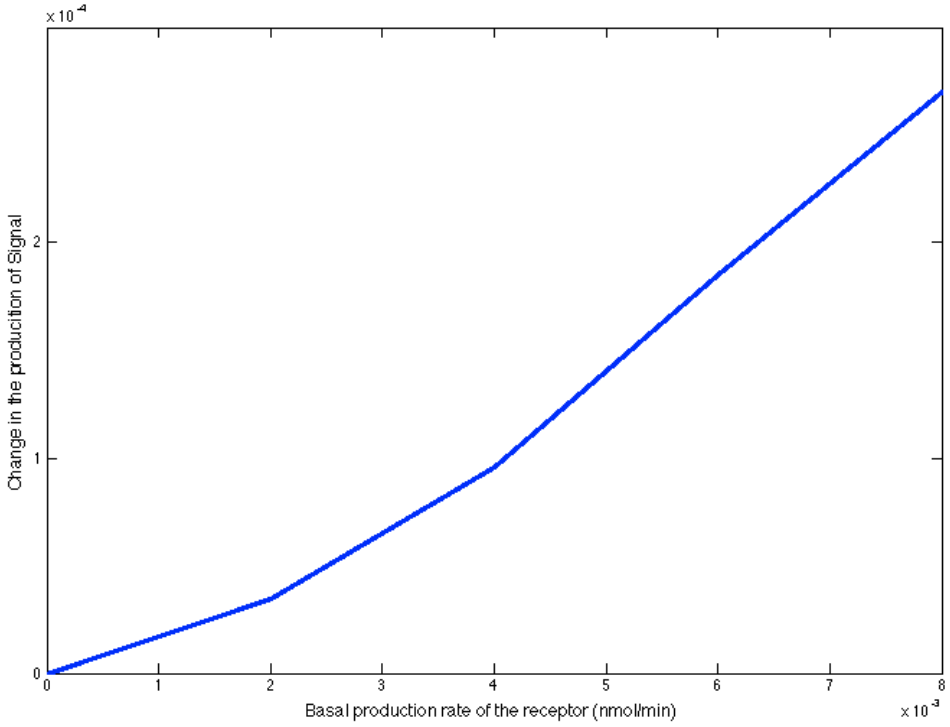
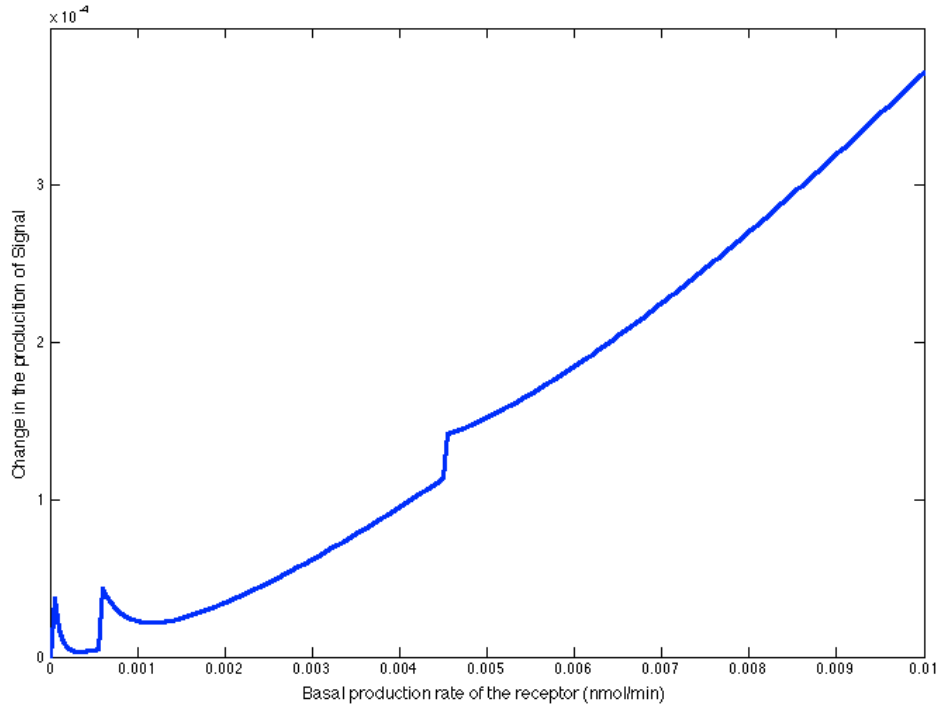
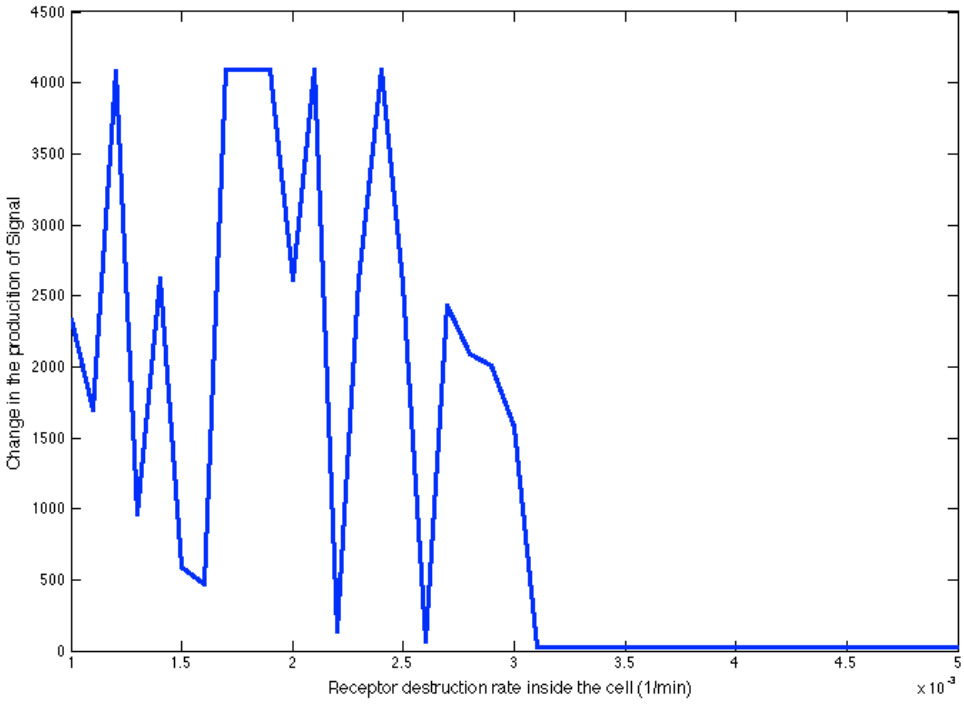


Graph 1 Lower Limit: 0 Upper Limit: 0.08



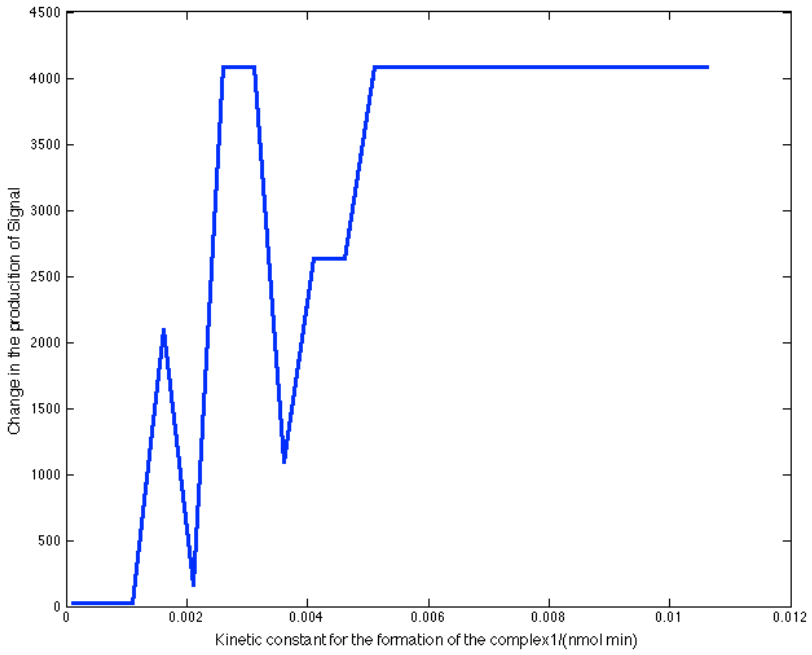
Graph 2 Lower Limit: 0 Upper Limit 0.01

2. δ_R***: Receptor destruction rate inside the cell (1/min):*** The result obtained indicates that the signal production is very sensitive to the modification of this parameter in a range from 0 to 3 x10^{-3} 1/min, after this value the destruction rate is too high that the receptor cant's activate de system. The parameter doesn't show any meaningful variation when the lower and upper limits are changed.

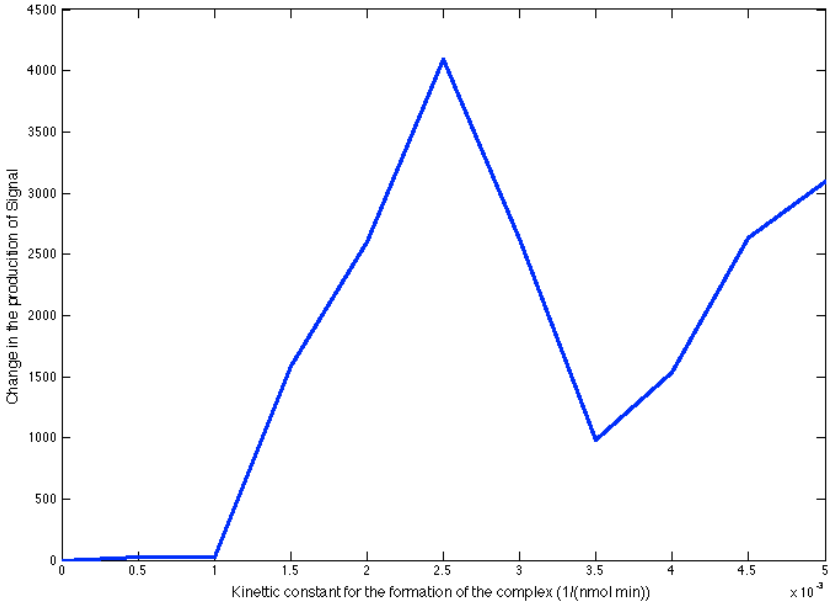


Graph 3 Lower Limit: 0.001 Upper limit: 0.005

3. ***mGRIR: Complex formation kinetic constant (1/umol min):*** The parameter has a significant influence in the response in a small range. Graph 4 shows us that after de kinetic constant value is 0.006 approximately the response is not affected by this parameter. Before this number the response varies in a lot .

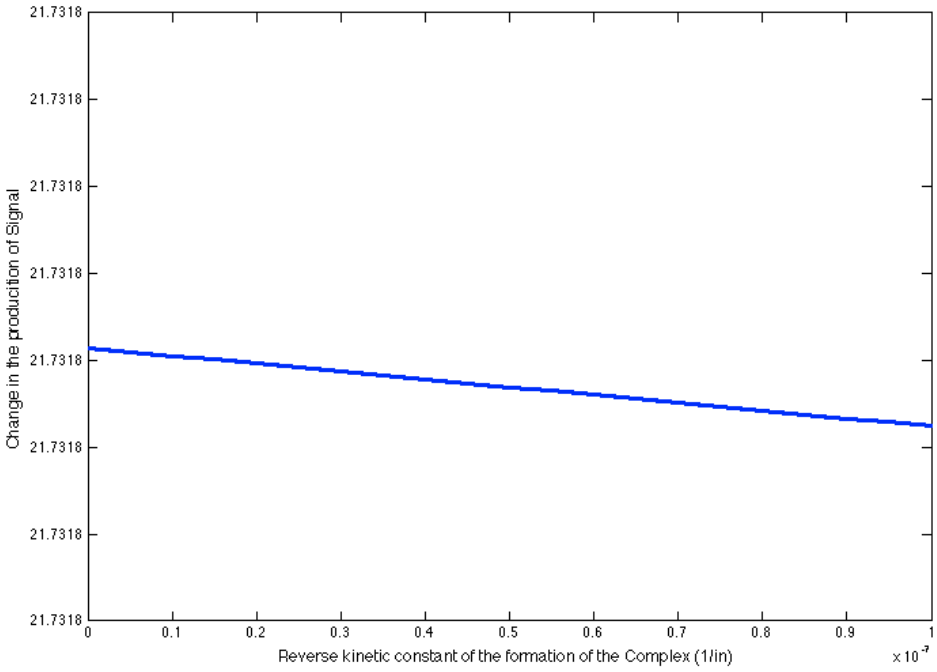


Graph 4 Lower limit: 1.08e-4 Upper Limit 1.08e-2



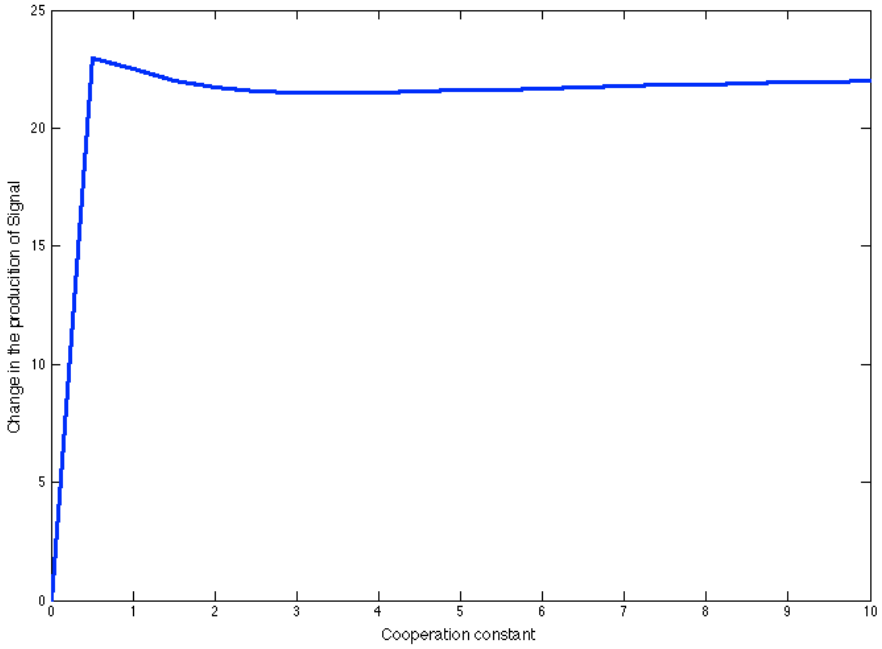
Graph 5 Lower Limit: 0 Upper Limit: 5e-3

4. ***mCC: Complex formation reverse kinetic constant (1/min):*** The parameter doesn't show any meaningful variation when the lower and upper limits are changed. The reverse kinetic constant of the formation of the Complex does not have effect in the change in the production; this can be due to the small order of magnitude of this parameter.

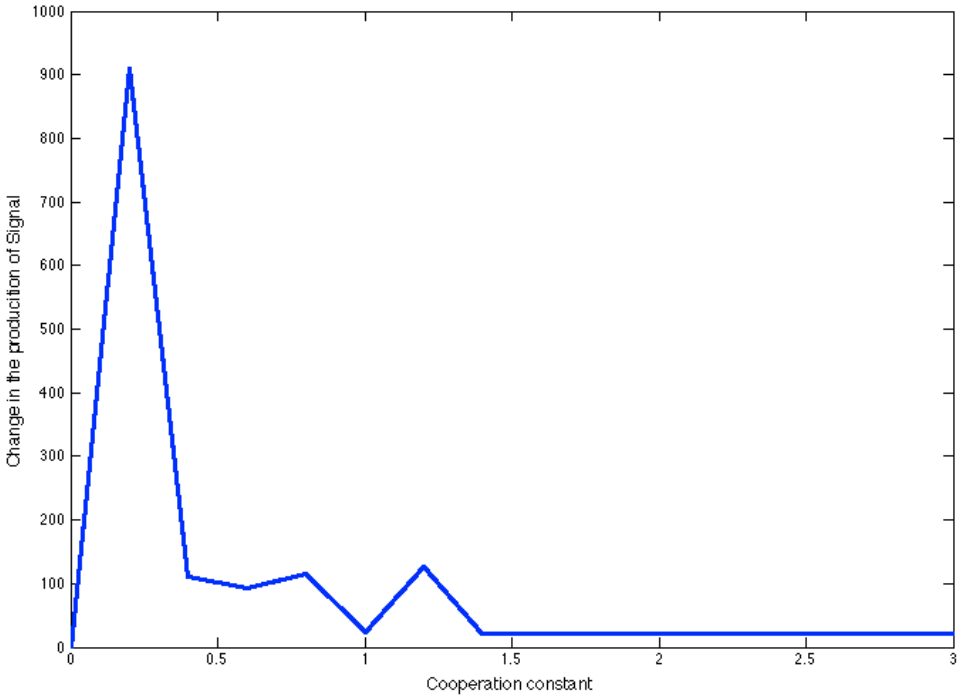


Graph 6 Lower Limit: 0 Upper Limit: 1e-7.

5. ***n: Hill coefficient (Cooperation):*** The effect of the cooperation parameter in the system response is almost insignificant after the value of three. Nevertheless is important to notice that between 0 and 2 the signal response is very sensitive.

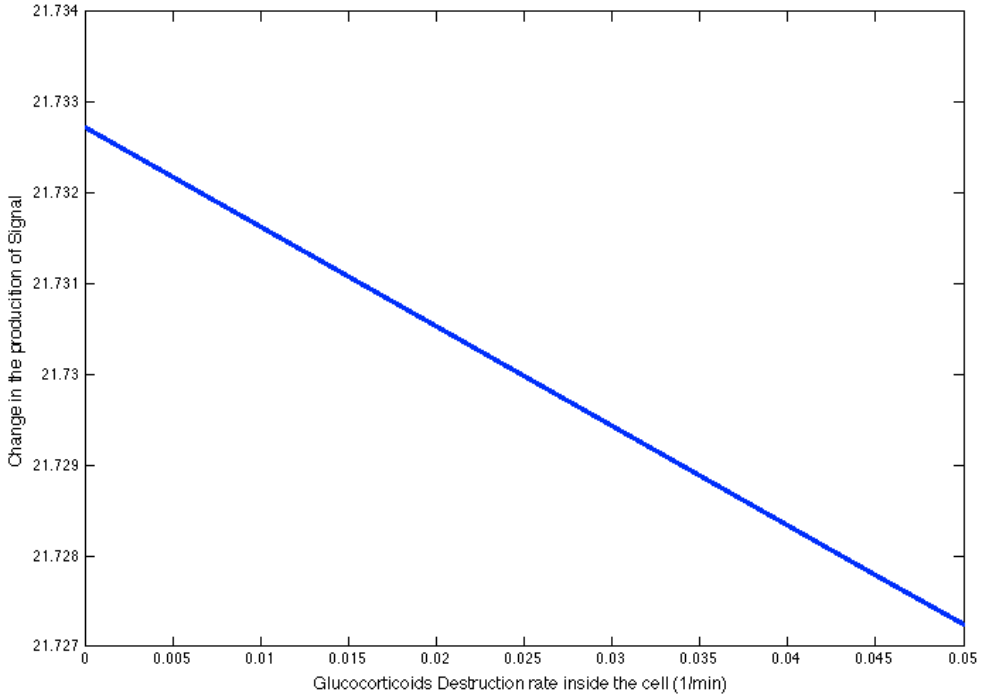


Graph 7 Lower Value: 0 Upper Value 10



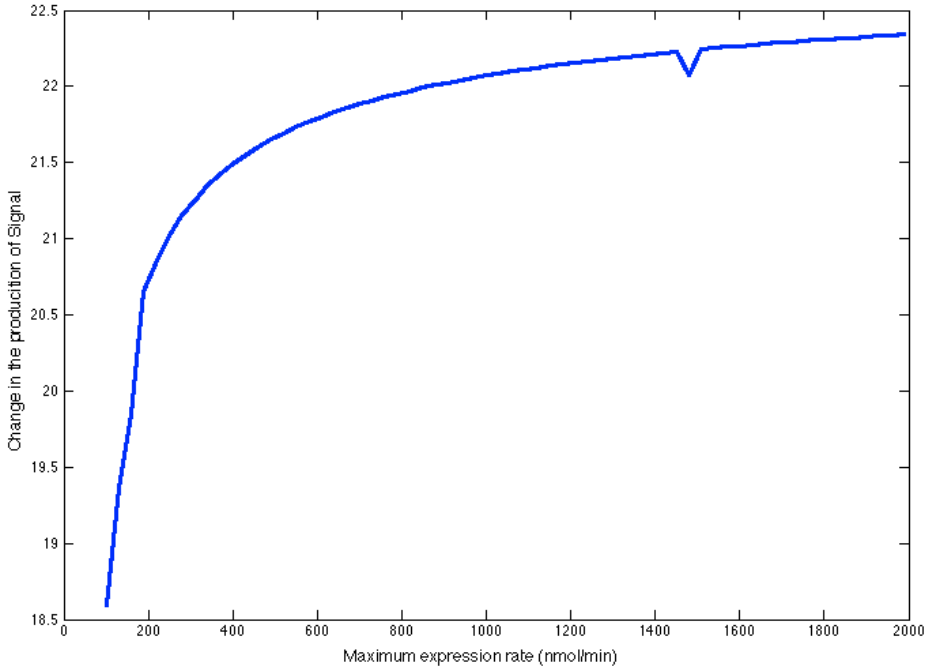
Graph 8 Lower Value: 0 Upper Value: 3

6. $\delta_{GRI:}$ ***Degradation Glucocorticoid inside the cell:*** Although there is variation when the upper and lower limits are changed, this change is minimum and therefore irrelevant for the response of the system.

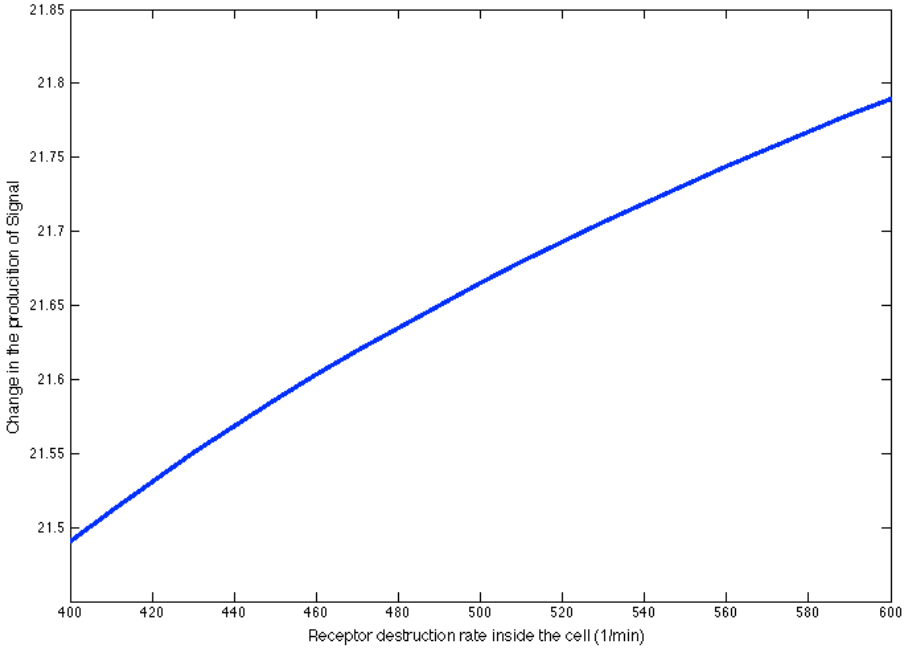


Graph 9 Lower Limit: 0 Upper Limit 0.05

7. ***β_{cc} Maximum expression rate:*** The parameter shows a proportional relation with the signal response until 600nmol/min (Graph 11) , then the response has not significant changes.

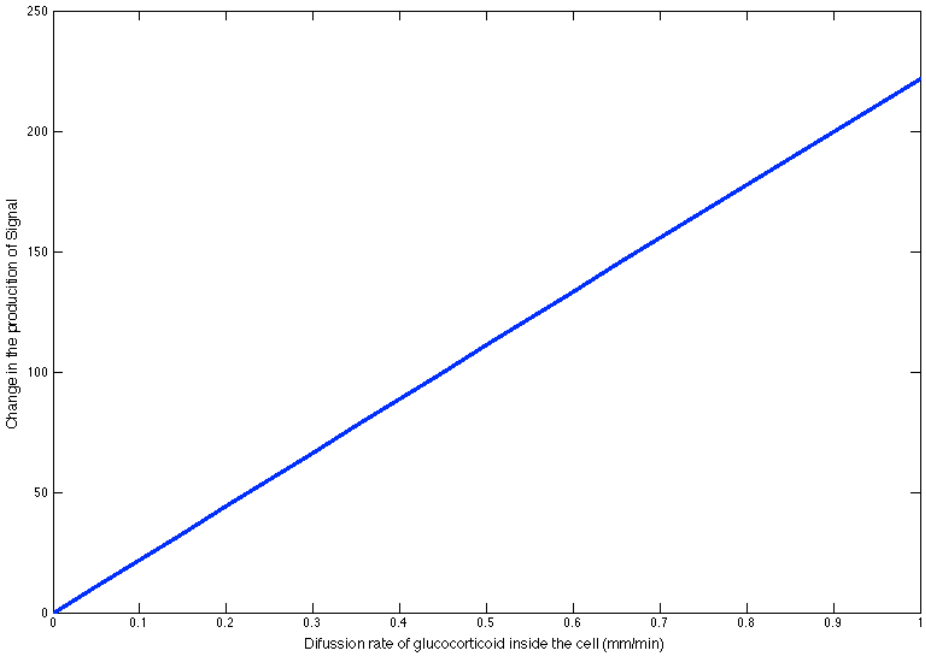


Graph 10 Lower Limit 100nM Upper Limit: 2000



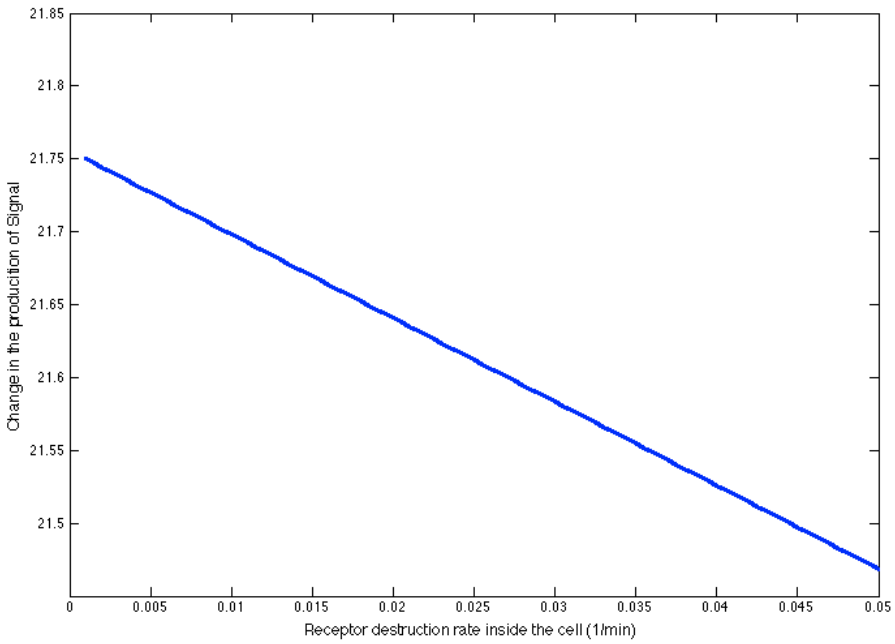
Graph 101 Lower Limit 400nM Upper Limit 600nM

8. γ_{GR}: ***Diffusion rate of Glucocorticoid inside the cell:*** The graph shows a straight line that tends to the infinite, with positive slope. The parameter has a strong influence in the response of the system.



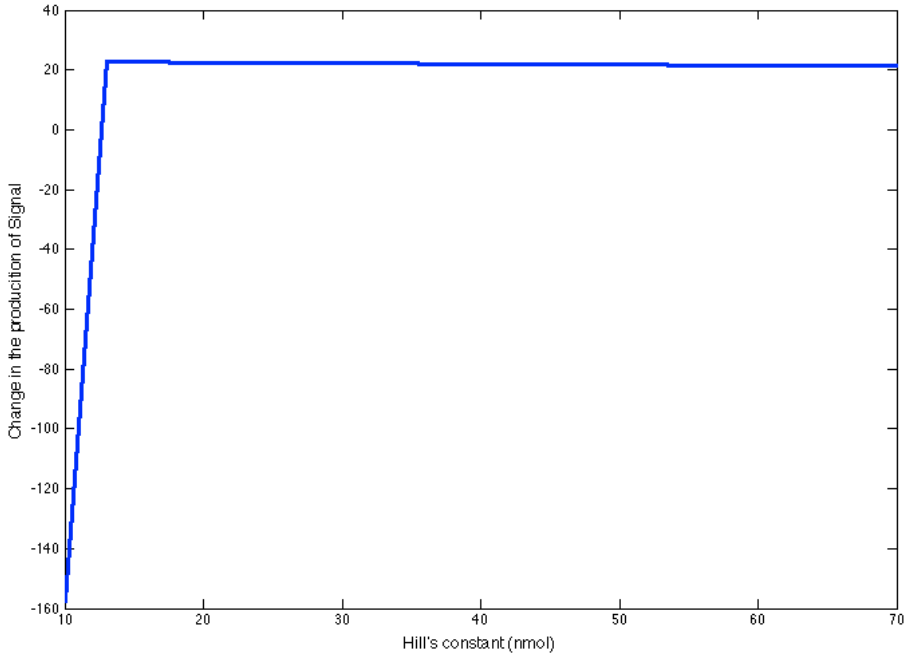
Graph 112 Lower Limit: 0 Upper Limit 1

9. δ_{CC} : ***Degradation rate of the complex:*** The graph shows a straight line that tends to zero with negative slope. Nonetheless the parameter doesn't show any meaningful influence in the signal.



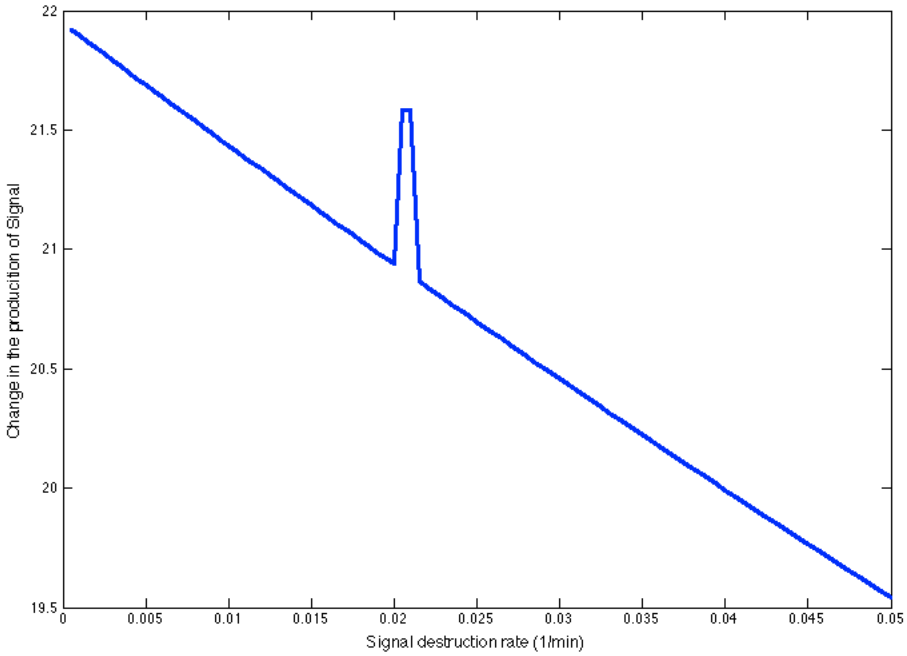
Graph 123 Lower Limit: 0.001 Upper Limit: 0.05

10. ***k: Hill's Coefficient:*** The graph shows an increasing behavior between 10 and 15 nmol, then it remains constant. Due to the fact that this is one of the unknown parameters, is important to notice that the gratest influence of this parameter in the system response is between 10 and 15nmol then the parameter screening should be done within this range.



Graph 13 Lower limit: 10 Upper Limit 70

11. ***δ_S Signal destruction rate:*** This parameter behaves in a decreasing way, with a little shock point in 0.02. The relationship between the system response and the signal destruction rate is inversely proportional, which makes sense because if the rate of destruction is too high the signal cannot been seen



Graph 14 Lower Limit: 0.0005 Upper Limit: 0.05