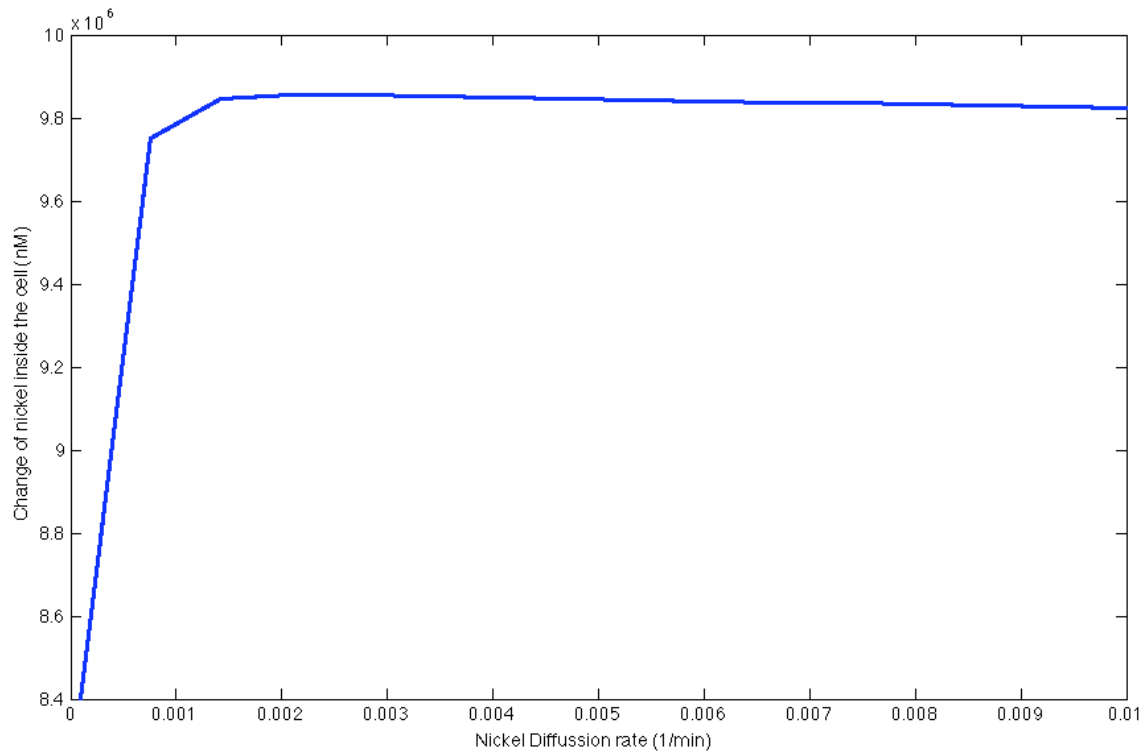


## SENSIBILITY ANALYSIS - NICKEL

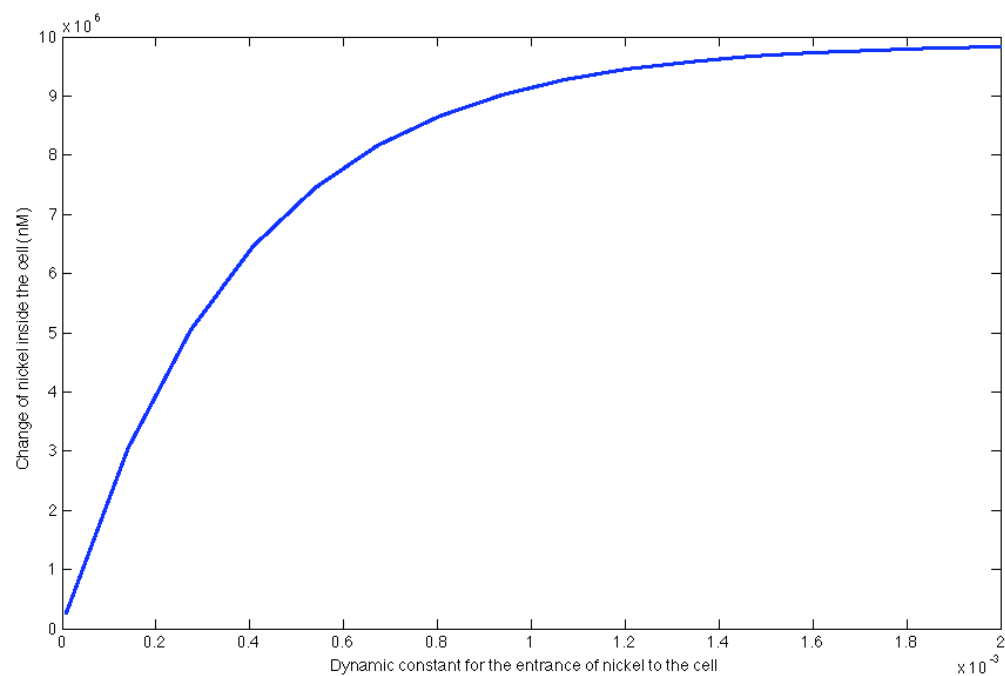
In order to see which of the parameters were the most relevant for the model we performed a sensitivity analysis. We took the values found in the literature and evaluated the model in a range that varied from one order of magnitude below the known value to one order of magnitude greater.

**1.  $\gamma_n$  Diffusion rate of Nickel :** The intake of nickel to the cell depends on the diffusion rate of nickel because this is the first way of entrance of the molecule. As seen below this parameter has a significant effect until 0.0015, after this value the response of the system has no effect by the diffusion rate.

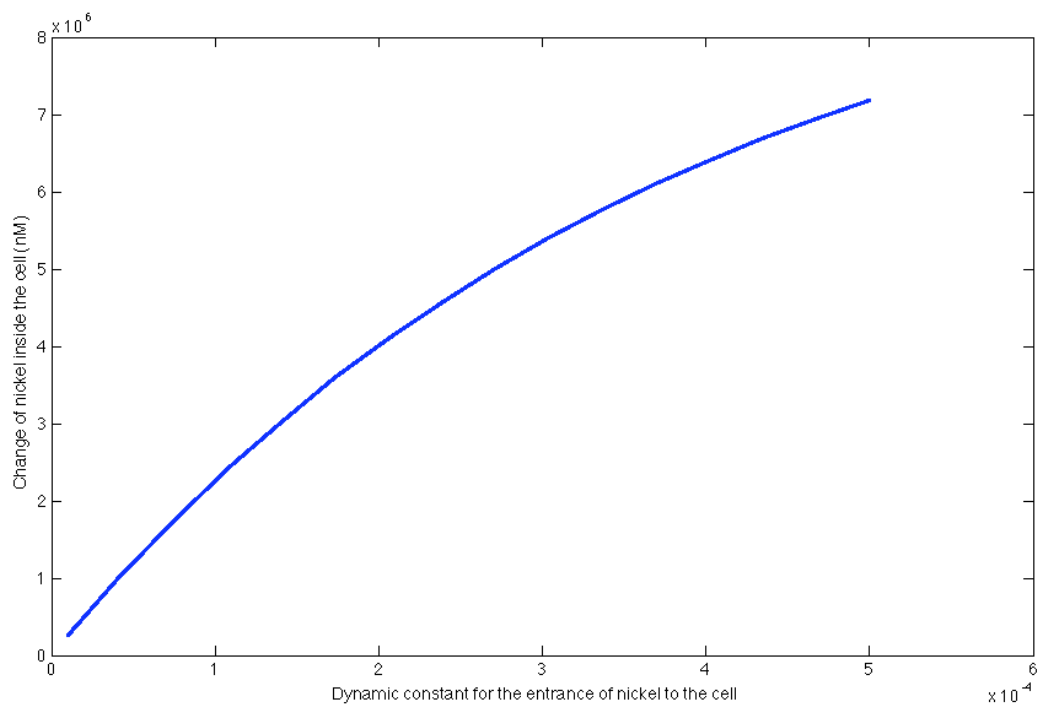


Graph 1 Lower Limit: 1e-4 Upper Limit: 1e-2

**2.  $k_p$  Dynamic constant for the entrance of nickel to the cell:** The graphs 2 and 3 show how the intake of nickel is higher when the dynamic constant of entrance is greater but this behavior stops approximately at 1, where the response of the system tends to have no effect by the change of the parameter

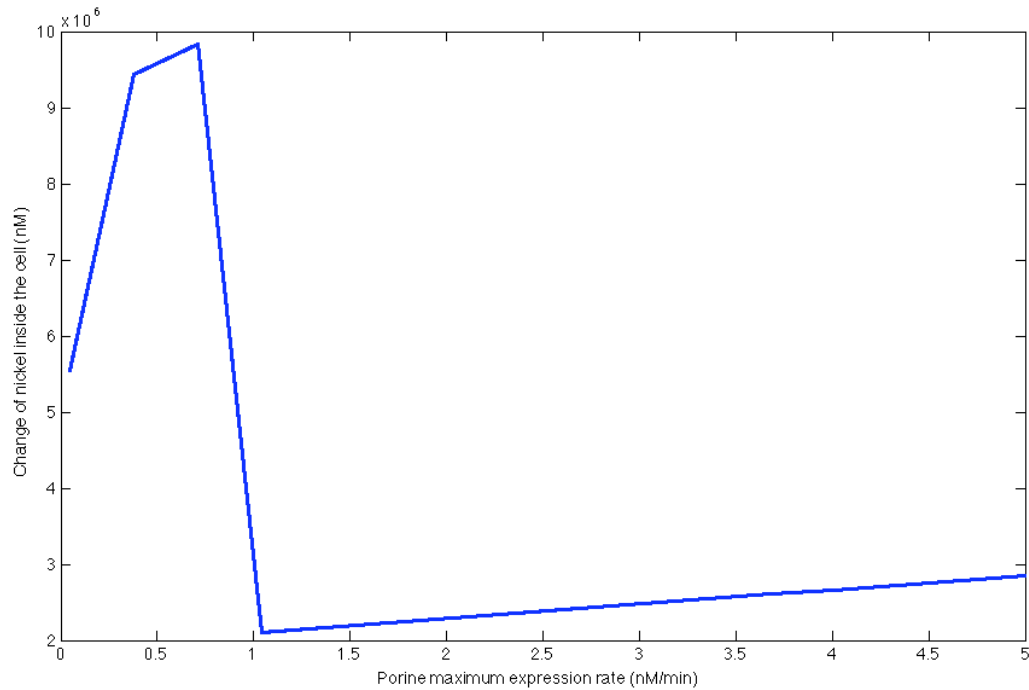


**Graph 2 Lower Limit: 1e-5 Upper Limit 2e-3**

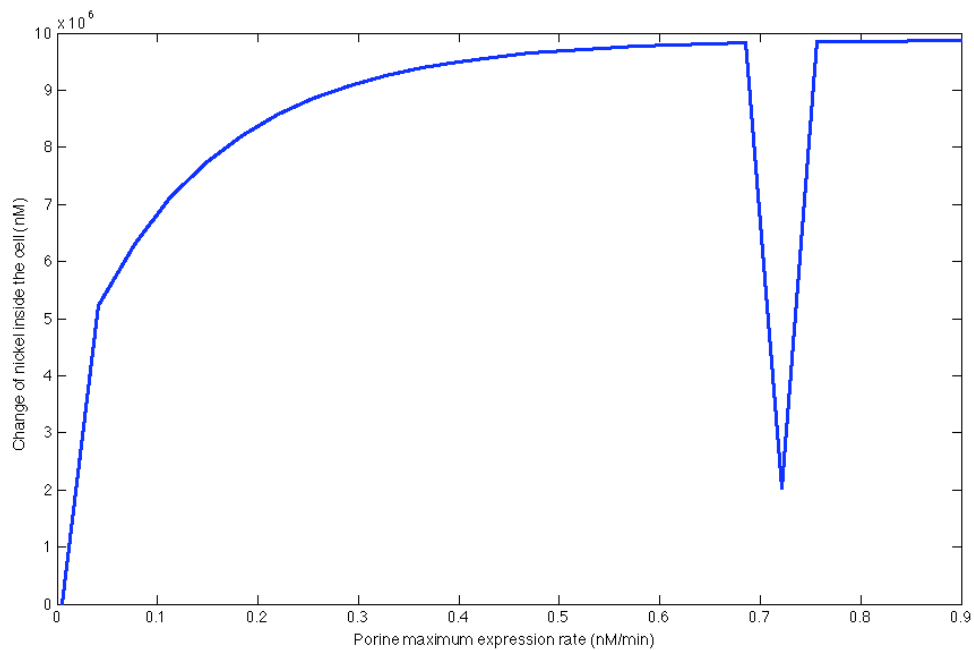


**Graph 3 Lower Limit: 1e-5 Upper Limit 0.5 e-3**

**3.  $\beta$  Porine maximum expression rate:** Graphs 4 and 5 show the particular behavior the maximum expression rate. The value of this parameter has a strong effect on the response of the system. The value of this parameter can be modified at the lab so it is necessary to screen it and find the perfect value for the nickel removal system.

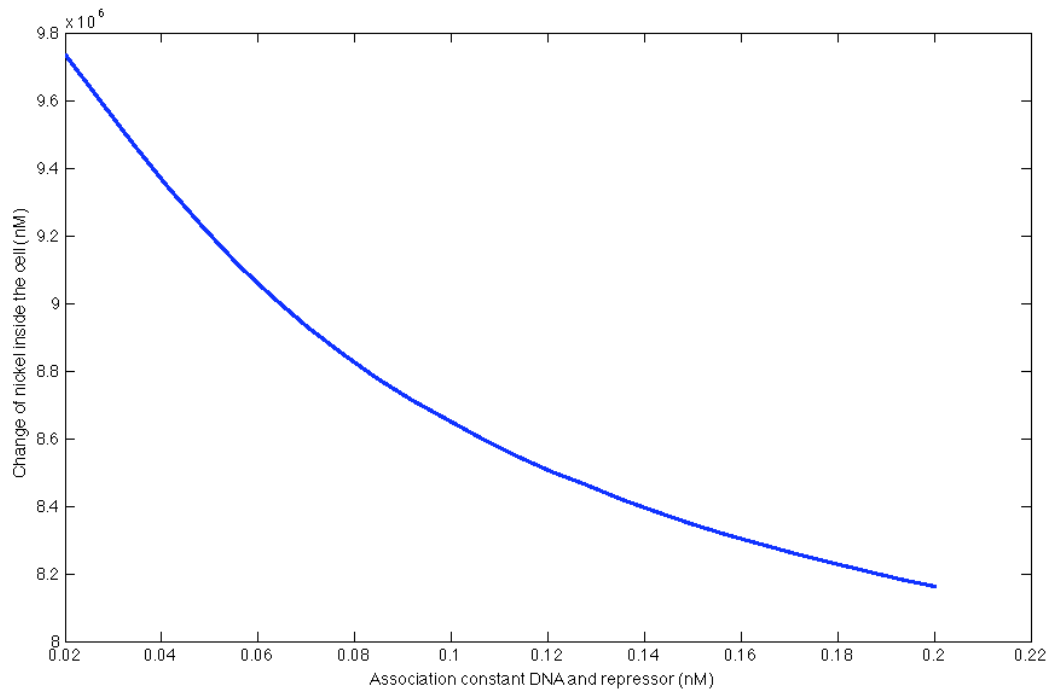


**Graph 4 Lower Limit: 0.01 Upper Limit: 5**



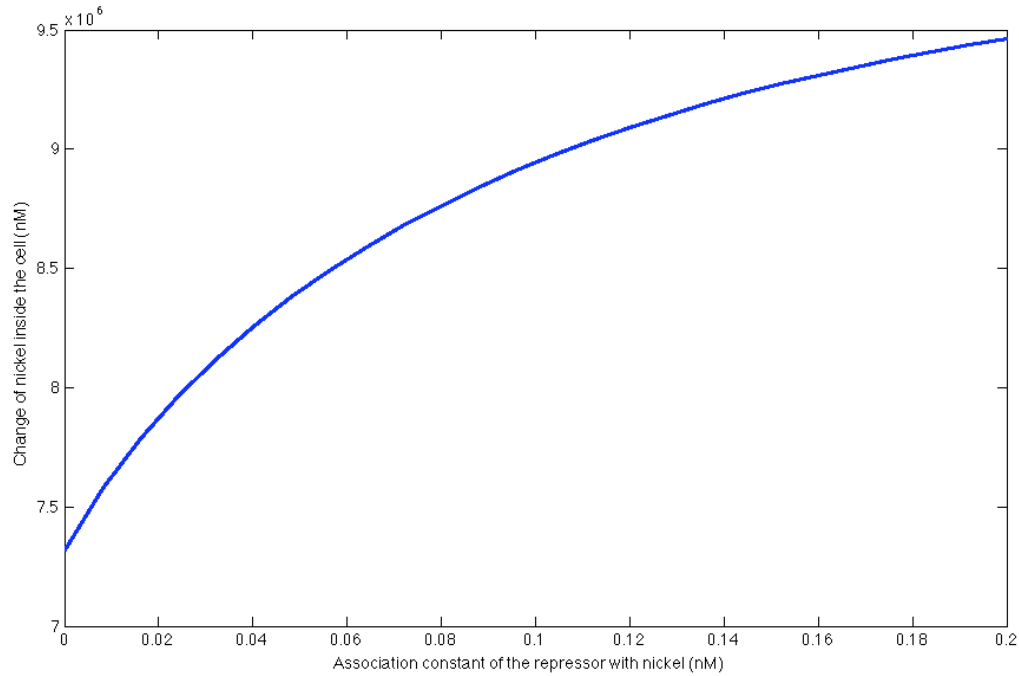
**Graph 5 Lower Limit 0.005 Upper Limit: 0.9**

**4.  $k_d$  Association constant DNA and repressor:** Graph 6 shows an inverse relation between the change in nickel concentration and the association constant of the repressor with nickel. If the constant is higher it will be more difficult to release the repressor and produce the porine making the entrance of nickel difficult.



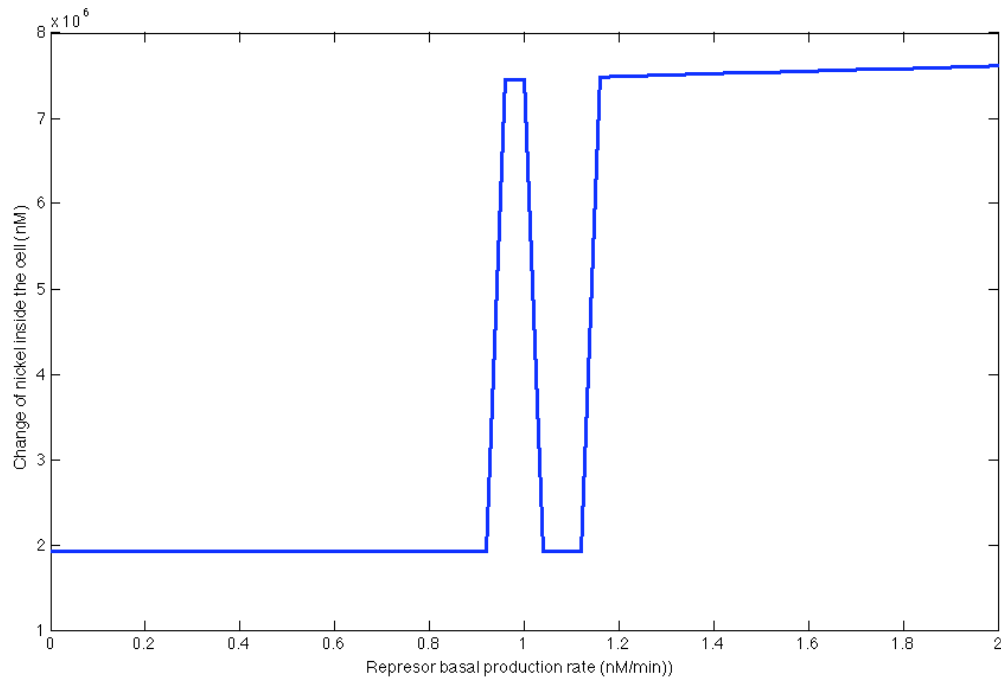
**Graph 6 Lower Limit: 2e-2 Upper Limit 2e-1**

**5.  $k_x$  Association constant of the repressor with nickel:** Graphs 7 shows a proportional relation between the association of the repressor with the nickel and the intake of nickel in the cells. If this constant is higher it means that the repressor will be released faster, making quicker the entrance of nickel through the porine.



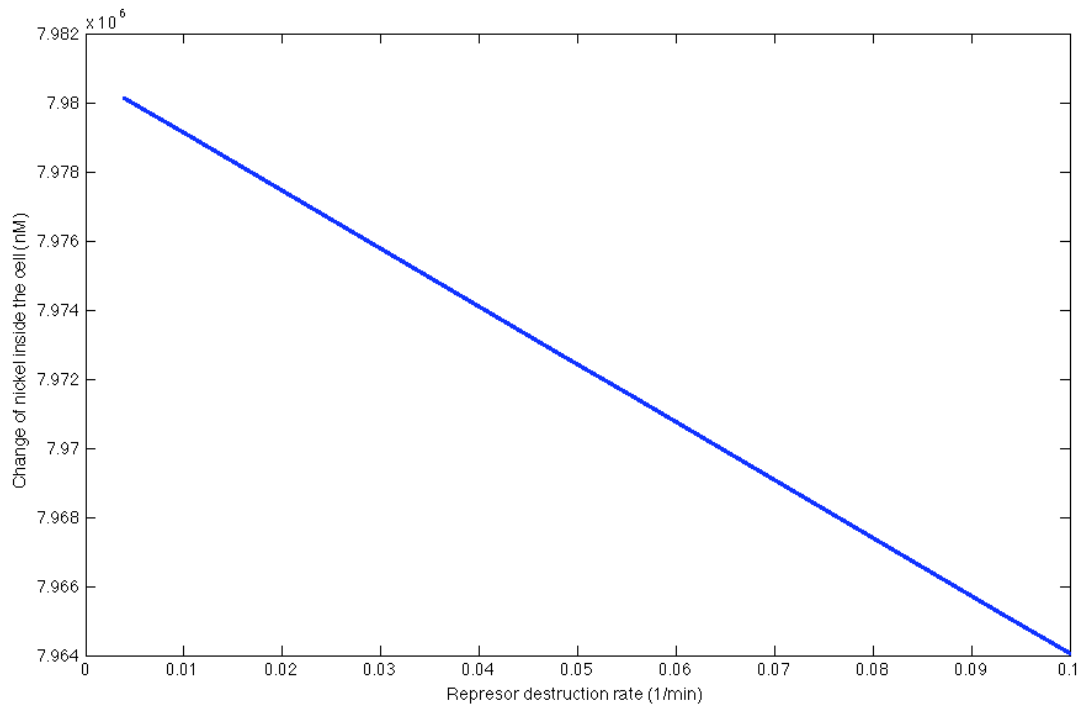
Graph 7 Lower Limit:  $2e-4$  Upper Limit 0.2

**6.  $\alpha_r$  Repressor basal production rate :** As can be seen in the Graph 8 the basal production rate of the repressor has a strong influence on the response of the system in a small range (0.8-1.3). After 1.4 the response of the system is no influenced by the change of the basal production. The parameter can be picked after 1.4 because it has no significant influence in the response and the intake of nickel is high enough.



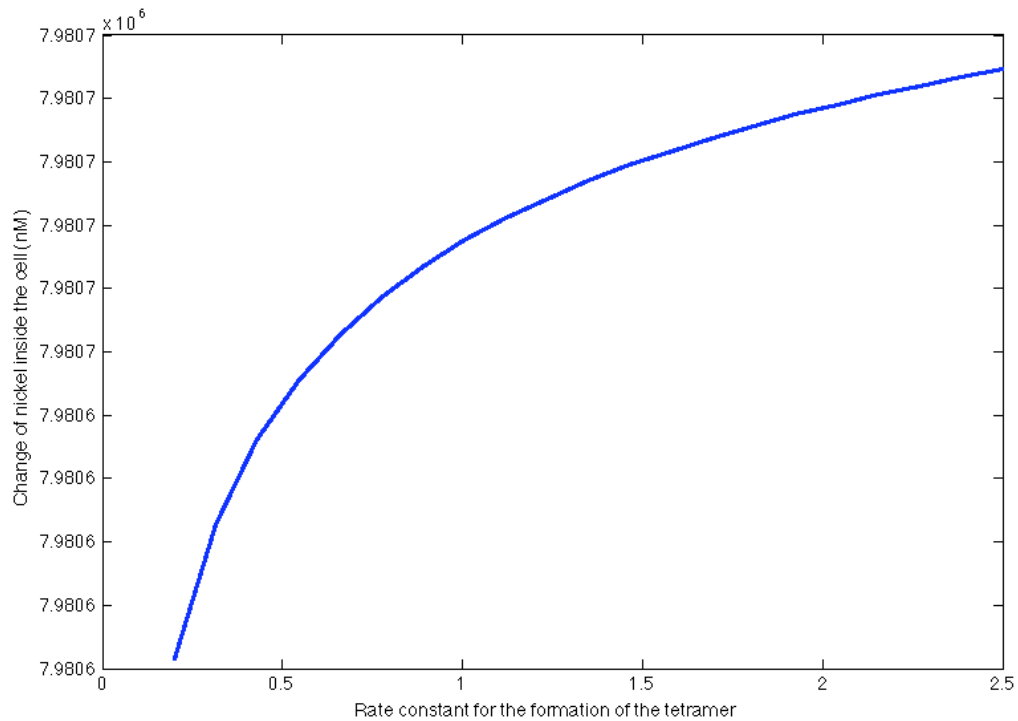
Graph 8 Lower Limit:  $1e-5$  Upper Limit 2

**7.  $\delta_r$  Repressor destruction rate:** This parameter has not a significant effect on the intake of nickel inside the cell, the change of the nickel intake is insignificant compared with the change that the other parameters had had.



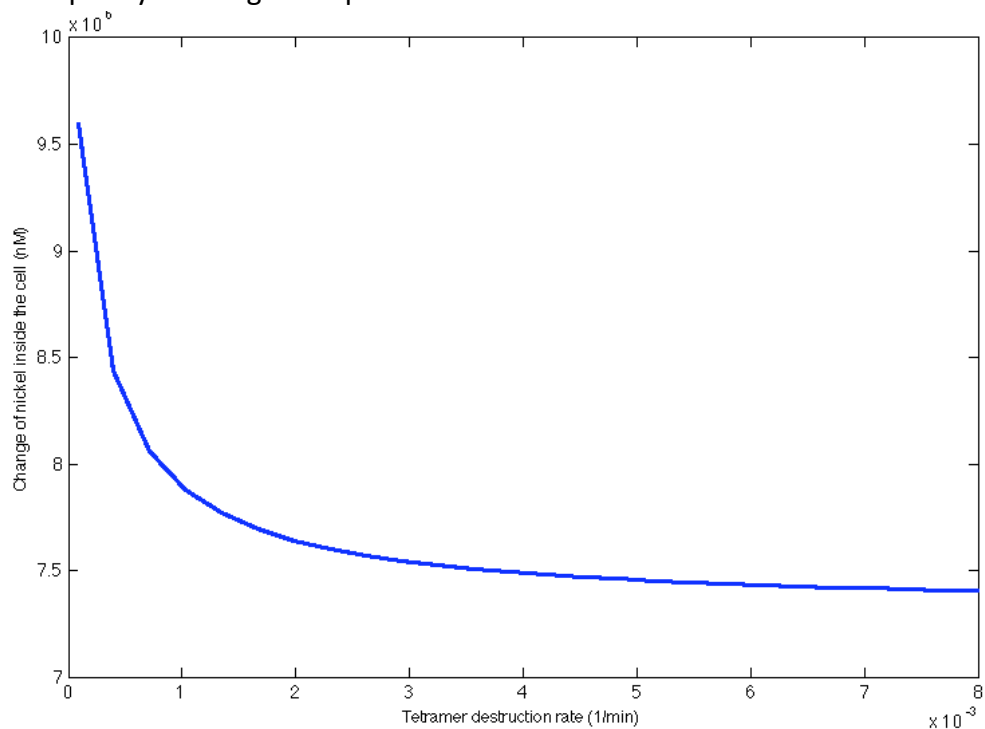
**Graph 10 Lower Limit: 1/12000 Upper Limit:1/120**

**8.  $k_t$  Rate constant for the formation of the tetramer :** As can see below the formation of the tetramer has no significant effect on the intake of the tetramer, this can be due to the fact that the constant has a high value and in the time scale we are managing the formation is too quick and it has no effect.



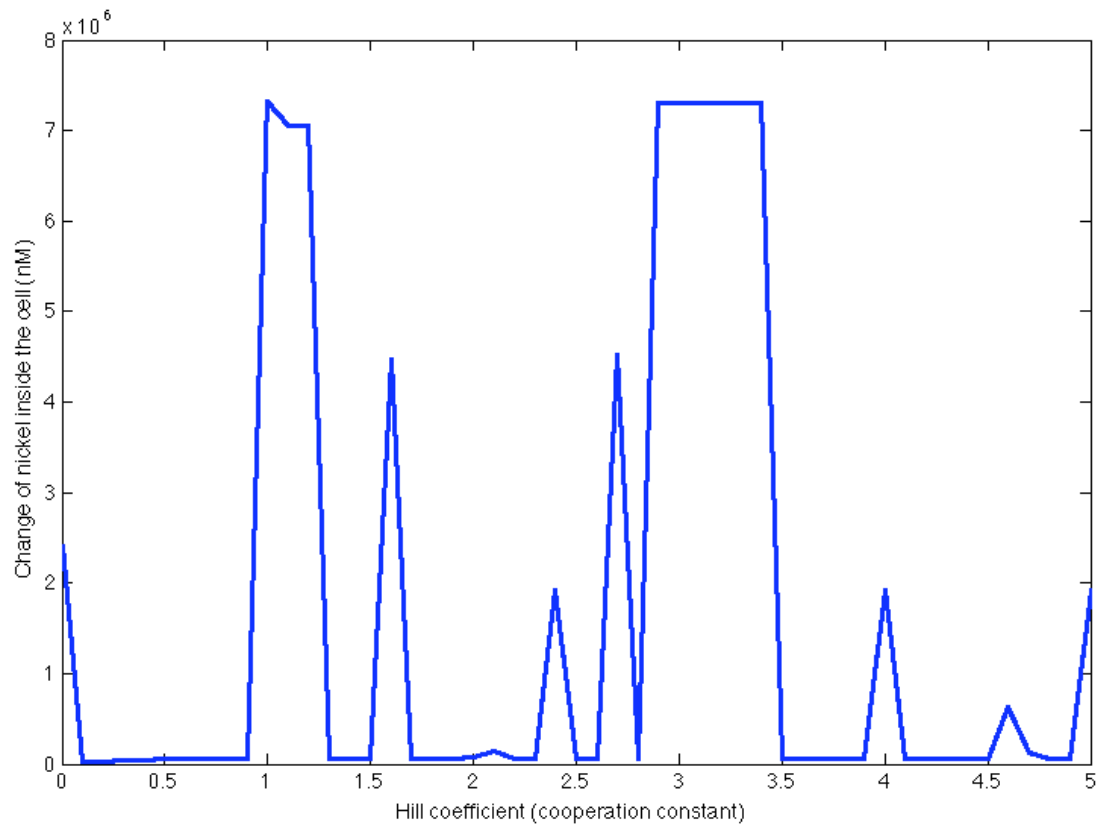
**Graph 11 Lower limit: 0.2, Upper limit: 2.5**

**9.  $\delta_t$  Tetramer destruction rate:** As can see below the tetramer destruction rate has an effect on the nickel intake. As the value of the parameter increase the repressor forms more quickly making less probable that the tetramer is not bounded to the DNA.



**Graph 12 Lower limit: 1/12000 Upper Limit: 8e-3**

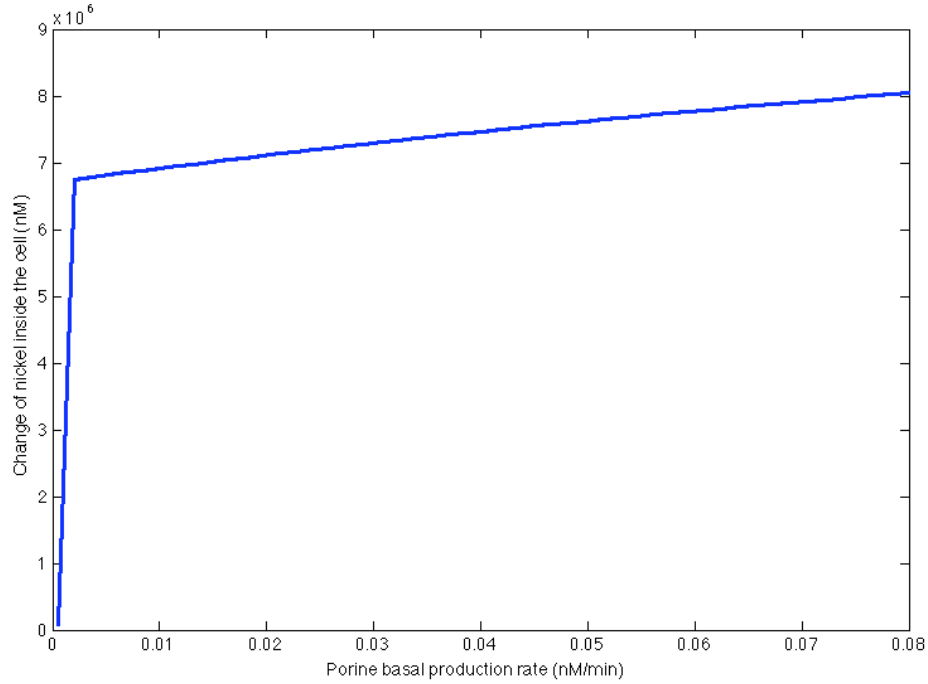
**10.  $n$  Hill coefficient:** Graph 13 shows the particular behavior of the Hill Coefficient. The value of this parameter has a strong effect on the response of the system. The value of this parameter cannot be modified at the lab, but the maximum expression rate does. If these two parameters are screened together it may be possible to find a value for this parameters with the desired response.



Graph 13 Lower Limit: 0 Upper Limit: 5

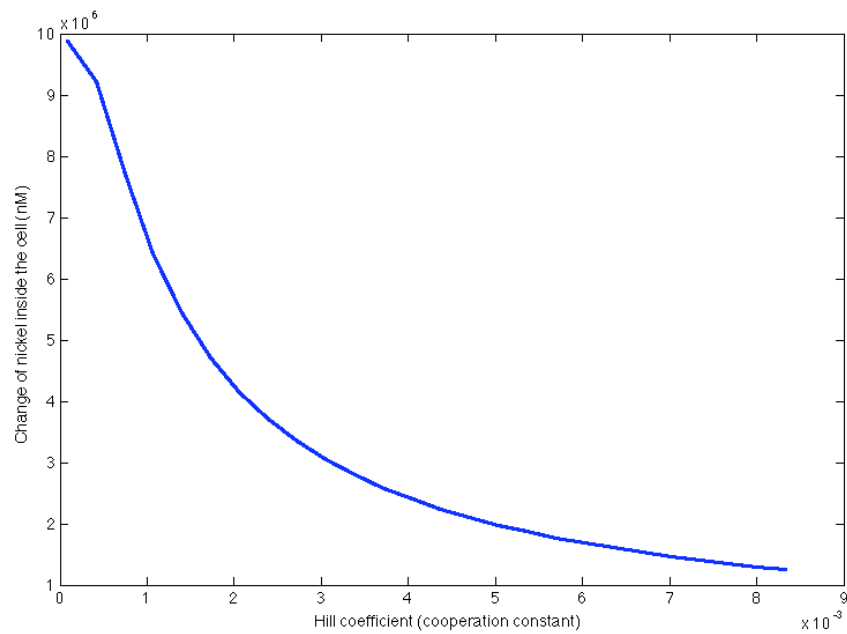
**11.  $\alpha_p$  Porine basal production rate:** Graph 14 shows that the basal production rate of the porine has a strong effect on the response of the system in a small range. After it take the value of 0.01 the change of the response of the system changes a little with the change of the parameter.





Graph 14 Lower Limit:  $5e-4$  Upper Limit:  $8e-2$

**12.  $\delta_p$  Porine destruction rate.** The change in nickel intake decreases as the parameter increases, which makes sense because if there is no porine the intake of nickel will be due to diffusion and this happens in a low rate, making the system unviable.



Graph 15 Lower limit:  $1/12000$ , Upper limit:  $1/120$