**List of simulations to do to characterize the behavior of receptor-only part of the model.**

1. Long application of glutamate (600 sec). Record final values for G, G\*,Gd1, Gd2. Plot them as a function of glutamate level in separate graphs.  
  
2. You were planning to do something similar, so maybe you have it already.

2a.  Long bath (square pulse of glutamate, 150sec duration, value of glutamate =5), followed by same one X sec after the first one ends. Record for G\*: Max(G\*) in response to the second pulse, the value of G\* at the end f the second pulse, total (integral) of G\* during the  
second pulse. Plot these as a function of X in three different graphs.

2b. Repeat 2a with glutamate amplitudes equal to 10, 15, 20, 30, 40, 50. Add the curves to the same graphs as 2a in different colors.  
  
3. Same as 2 (both a and b) with pulse duration of 30 sec.  
  
4. Same as 2 (both a and b) with pulse duration of 50 sec.  
  
5. Same as 2 (both a and b) with pulse duration of 100 sec.  
  
6. Apply 10 brief square pulses (500 microM amplitude, .06 sec duration). time between pulses Y=5sec.  Do change MaxStep to be a smaller number! 0.005 might work. It will slow down the simulation, unfortunately. Record G\* maximum value in response to 1st,2nd,3rd and last pulse (4 points in graph 1). Record jump in G\* in response to first, second, 3rd and last pulse (4 points in graph 2). Record the largest value of Gd1 (a point in graph 3) and the largest value of Gd2 overall (a point in graph 4). In each graph the horizontal axis is Y.  
  
7. Repeat 6 with different values of Y, adding points to the graphs. Increase Y in 5 sec increments until the graphs 1 and 2 flatten out.  
  
8. Do 6 and 7 with exponential pulses instead. Choose the parameters of the exponents so that the integral of glutamate in each pulse is about the same as in the square pulse (500\*.06).

**Overall plan for this part of the project (for the full model, receptor part and integrated with the calcium model)**

1. Explore receptor part of the model and it desensitization.

Only use the part of the model that up to G\*.

a) apply constant glutamate, report G\*(t) at different levels of glu. (pick 4-5 different levels, starting with where desensitizaton is minimal, to where it's strong)

b) Parameter variations to report changes in G\*(t) as you change parameters:

- increase k\_d and k\_r to make the desensitization 1 pathway faster

- decrease or increase epsilon and influence of G\* up or down to make the second desens. pathway faster or slower

- turn off the second desens. pathway

This will help tune parameters of the glutamate receptor model, but hopefully also give us a figure on the properties of this part of the model

2. Look at Ca feedback on IP3 degradation. Use full model. Choose three string glutamate pulses (short, medium and long). Reduce the strength of Ca feedback (there are two parameters: A (max. to be reduced) and K (turn-on threshold. To be increased)) and note the effect on IP3(t) and Ca(t) in response to the three chosen pulses. End up with fixing the strength of feedback at a resonable level, where it is present, but doesn't dominate the dynamics. Finally, go back and get rid of the Ca feedback on IP3 degradation and redo all the simulations to see if it changes things



3. Short Glu pulses. Hopefully in this art we'll be able to confirm that we still have the diversity of Ca responses, and that their properties are aligned with experimentally recorded ones.

a) vary glu pulse parameters as before. Each time record Ca(t), IP3(t). We might also want to look at Ca response types, total calcium (area under the curve), Max Ca, Ca duration.

Make figure similar to the last one in your report (response types color coded in the glu parameter space).

Make figure similar to Fig 4 in Taheri et al.

Show IP3(t) and Ca(t) for about 10 examples from different response types and different parts of the parameter space.

b) Same thing, but for each glu run also randomly pick parameter values for all pars in G\*-to-IP3 part of the model (randomly chosen uniformly in the interval default value +/- 10%). Make the same figures + the bar graph of response types.

c) same thing, but now the parameters are also randomly chosen in the Ip3-to-Ca part of the model in a way that corresponds to "processes" or "soma" in the last figure in Taheri et al.  Same figures as in b)

4. Bath application of glu (constant glu). Another check for the model - we want to compare with Fig 4D of [Xie et al 2012](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3499417/" \t "_blank).

a) Resord Ca(t) IP3(t) at different glu levels (all much lower than the maximum peak value in pulses). Report IP3 peak, IP3 duration, IP3 total, and the same for Ca as a function of Glu level.

b,c) vary parameters as in 3 b),c) above. report response type as well (with a modified classifier, ignoring LL responses)

5. Producing model predictions for what happens after bath washout. Pick glu pulse params that produce single-peak response.

a) Do a long bath of some glu concentration. Turn off bath. Apply pulse time t\_delay after the end of the bath. Record Ca peak, response type, duration, total Ca, as a function of T\_delay.

b) Repeat for different levels of bath glu