2) Written Comment of #2

a) Simulation Done in Julia, NOT written so refer to Q2 folder on Github link for Julia code

The plot will be in supplemental as Figure 1

b) Using Central Difference on the Code from part a, Scaled Sensitivity Coefficients were calculated

- See Q2 folder, The simulation run file generates all parts in the end

c) Rank order the importance of the species using SVD of a Time averaged Array

- Done to all phases

Part C Conclusions.

C) To better see the Difference refer to Figure_Compare.pdf in the Q2 folder, I will be explaining SVDs from that item.

The SVD rank order importance of species U gives an M x M combination matrix

This is asking for the importance of model species which I interpreted to mean the 3 genes in our system (P_1, P_2, P_3)

If I understand correctly, the first ABS valued colum will tell which species (in our case gene) is more important to the control of the circuit. So if species 1 has a higher 1st row SVD matrix value, it is important for control.

looking at the three ranked importance phase values I generated they appear as follows

Gene	Phase 1	Phase 2 early	Phase 2 late
Species 1	0.00279	0.431	0.452
Species 2	1.00	0.604	0.580
Species 3	0.0006036	0.670	0.678

c) Discussion

for phase 1) Species 1 does not contribute nearly Any while Species 3 contributes almost Nothing, Species 2 on the other hand contributes most of the control here and is the top of the ranking

for phase 2 early) In early phase 2 all of the species now contribute, but there is an order

Species 3 is the largest at ≈ 0.670, while Species 2 is less than species 3 but more than Species 1

for phase 2 late) This is after it has stabilized and the ranking remained the same as early phase 2, however the magnitudes chaged, with species 2 now contributing less than it did for phase 2 early while the other 2 increased in strength.

Overall as inducer was added we saw Species 2 Decline over the Different inducer levels, while species 3 and 1 increased as inducer was added.

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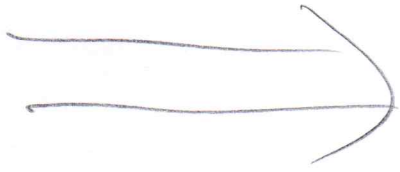
c) The reasoning I think for why there was a shift in ranking from phase 1 to 2 is The swap from a background expression and repression controled loop to a loop that relies on inducer level and kinetic saturation

in phase 1 there is no inducer, which means the levels are only governed by background expression, given that P_2 represses P_3, most of the control over species levels will be in P_2 exerting stray repression on P_3, while P_1 cannot contribute greatly due to not having any inducer.

i.e. P1 induces P2 and P3, while P2 represses P3, without inducer activity promotes P1 so most control occurs when P2 is repressing P3 background growth.

once inducer is added however now P_1 can contribute to the protein levels, and P_3 can become involed in the balace between P_2 repression and P_1 induction



C) I think that P_2 repression is not as strong as the power of the inducer, and so it begins to matter less (and thus falls in rank) while P_3 and P_1 rise as they modulate the inducer level into growth over time.

Conceptually here this is like a cell that wants to keep a system off almost completely until inducer is added,
The repression of P_2 is important to controll the back ground expression, however once inducer is added the system has the $P_1 \rightarrow P_3$ loop to by pass repression of P_3
however the presence of P_2 in late phase still tells me the cell wants P_2 to remain at a higher concentration than P_3 so that theoretically if inducer was removed P_2 could take control and prevent run away P_3.