Cell-cell Interaction and Pattern Formation

Workshop on Flags, Signalling and Landscapes

Friday 17/05/2024

<u>Presented by: Group 5</u>

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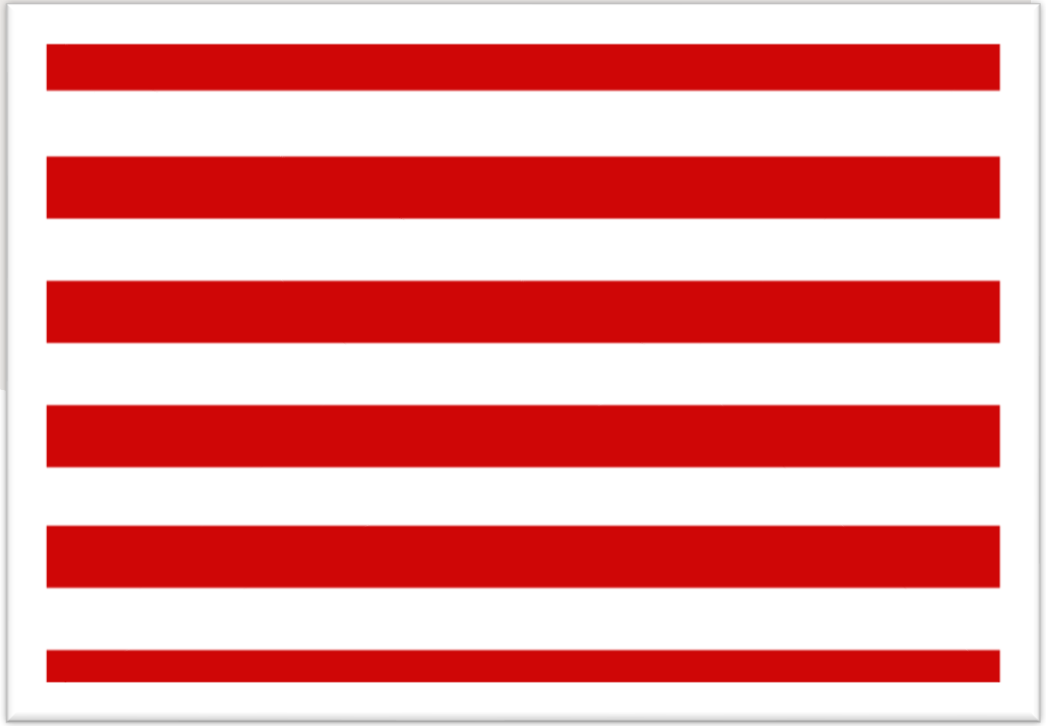
The Idea of Our Problem



- Consider a linear array of cells having two chemical morphogens A & B
- Both A & B can give the cells distinct fates of patterning
- Breaking the symmetry
- Can we get a network motif to do the same?

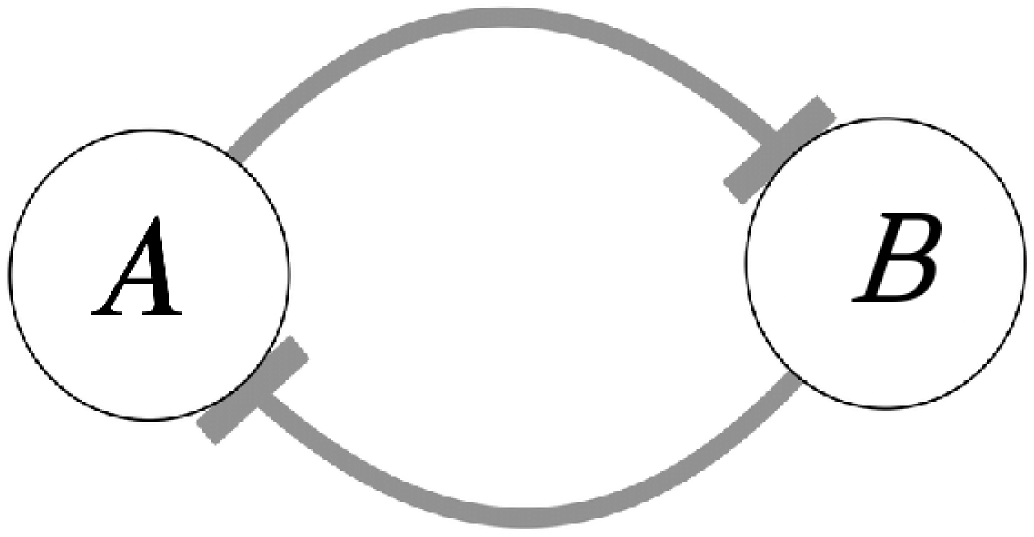
Patterns in Nature

Stripe patterns on the tail of Lemur and cats(of course)

Turing diffusion Patterns

Toggle Switch

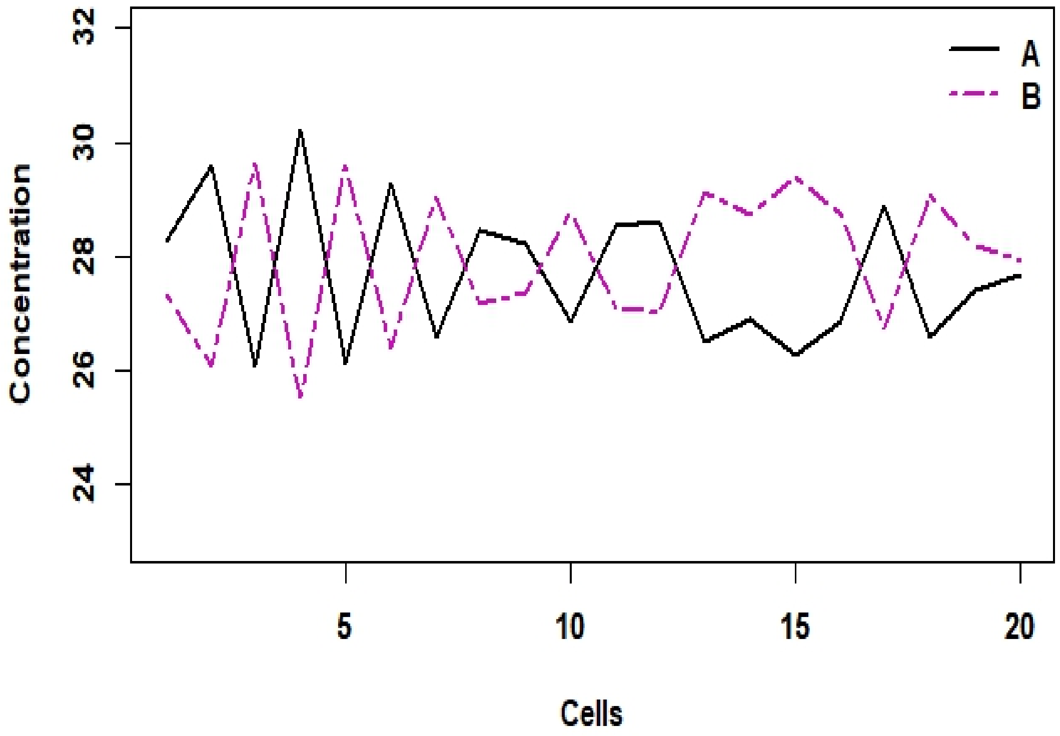
- Interactions are captured by simple hill's function
- Strength of repression of A and B is equal
- Every cell starts with the same concentration of A and B with some noise
- Noise breaks the symmetry for cell fate ?!
- Cell fate(color of cell) is decided at the steady state
- Fate of a cell is independent of its neighbor



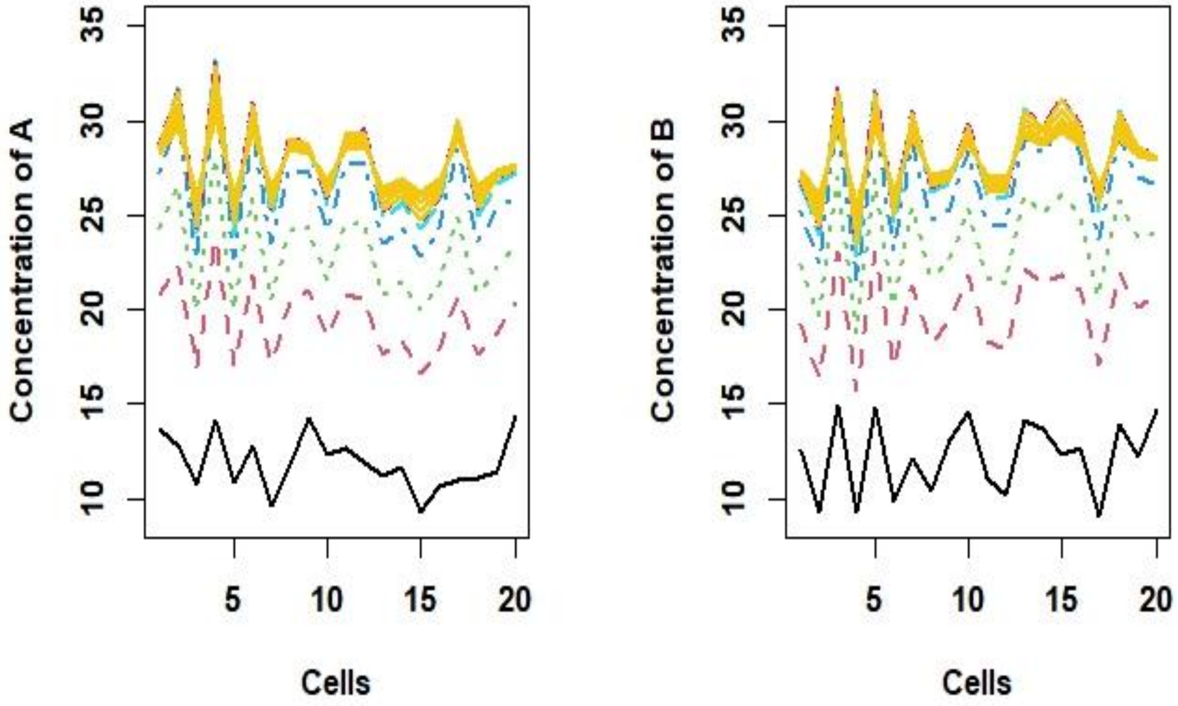
$$\frac{dA[t]}{dt} = \frac{\alpha}{(1 + (B(t)/K))} - \kappa_a A[t]$$

$$\frac{dB[t]}{dt} = \frac{\beta}{(1 + (A(t)/K))} - \kappa_b B[t]$$

Simulation Study

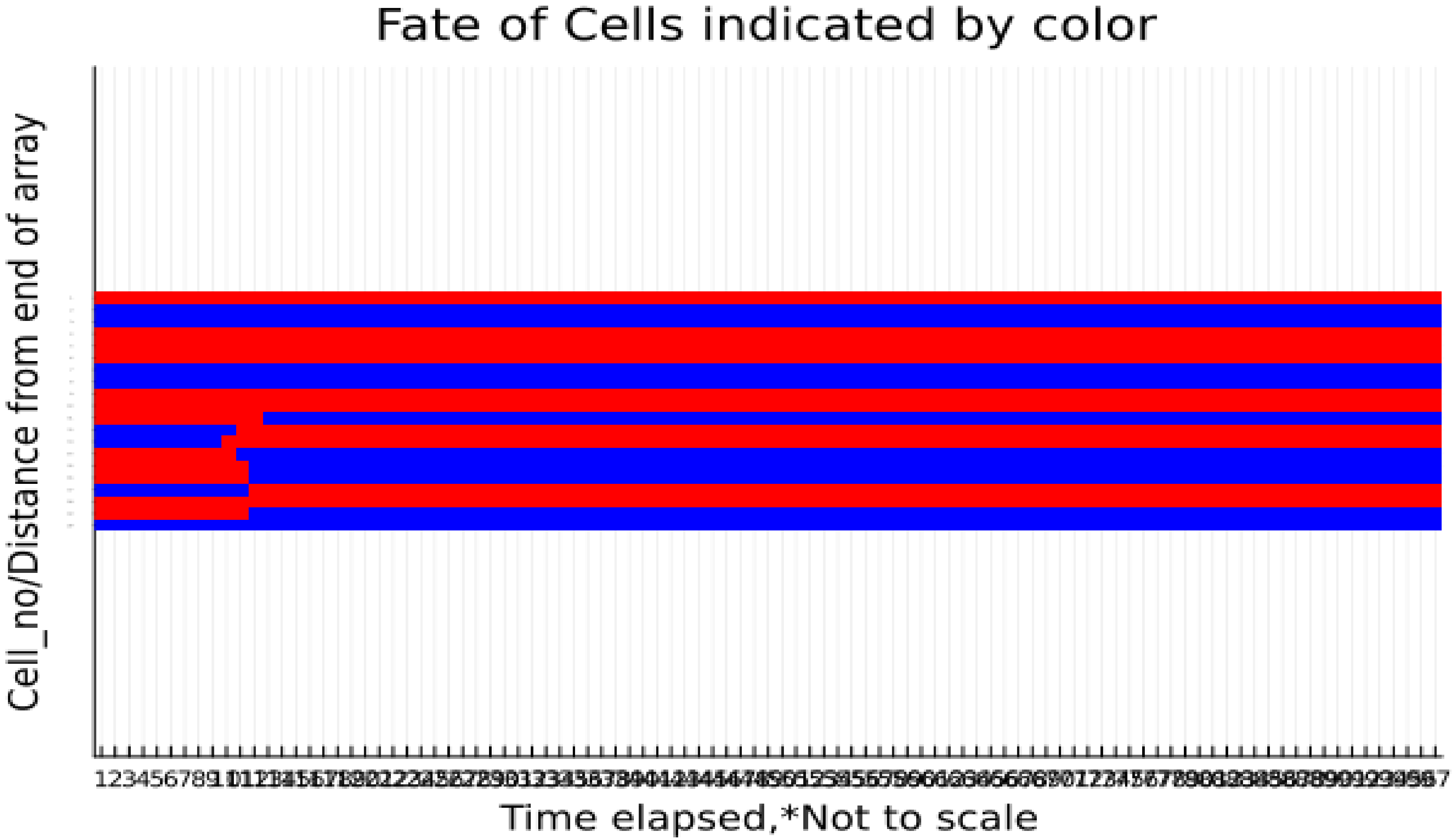


Concentration at Steady State

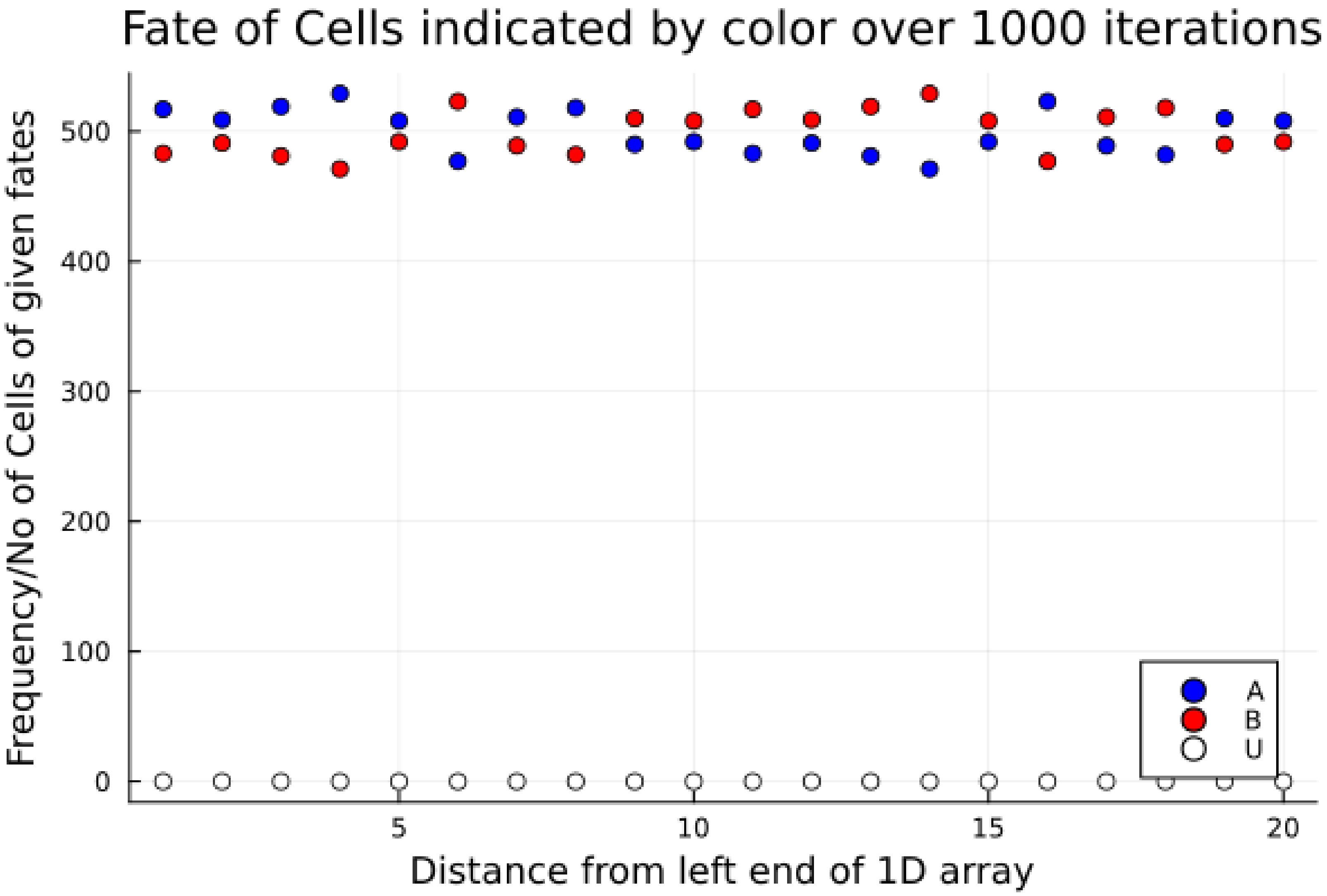


Concentration profiles with increasing time

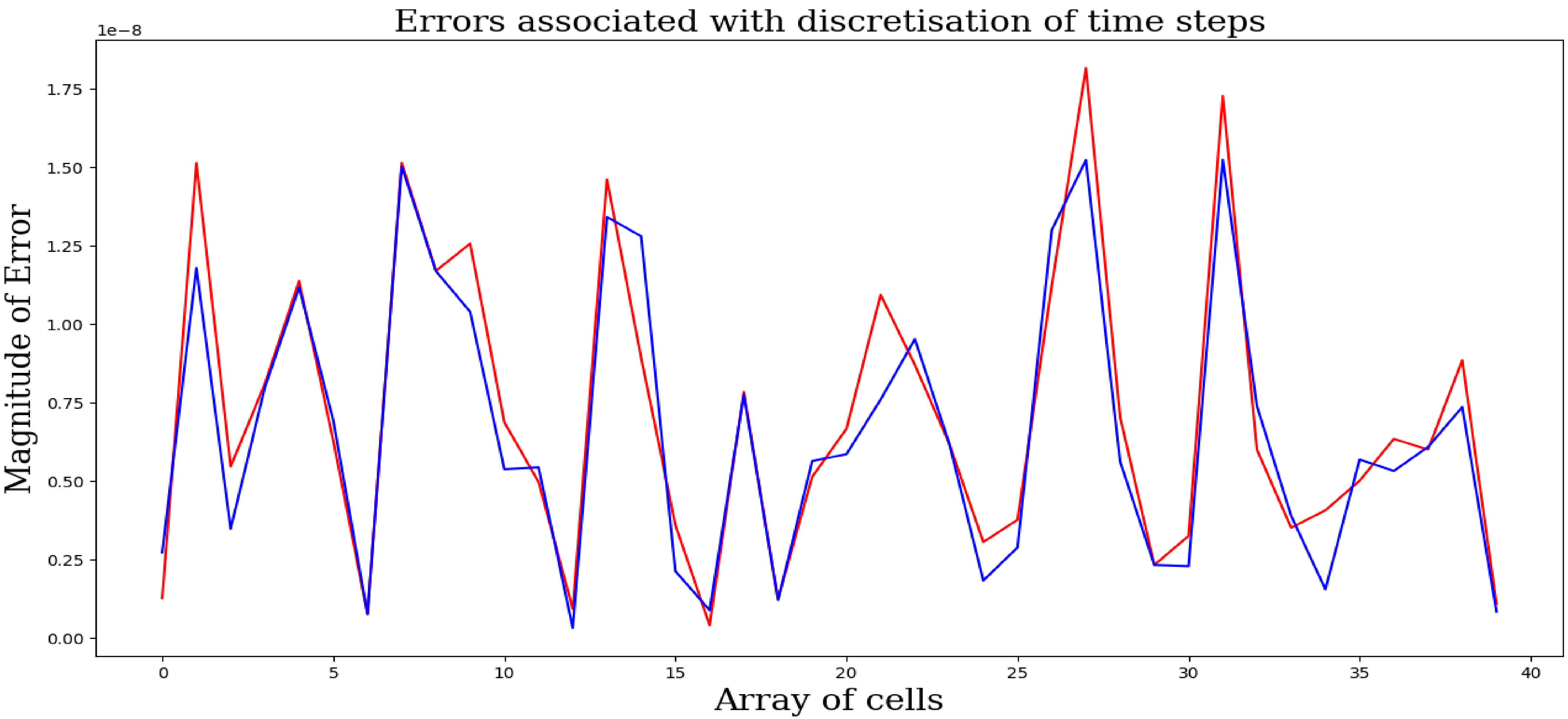
Spatiotemporal variation of cell fate for 20 cell array



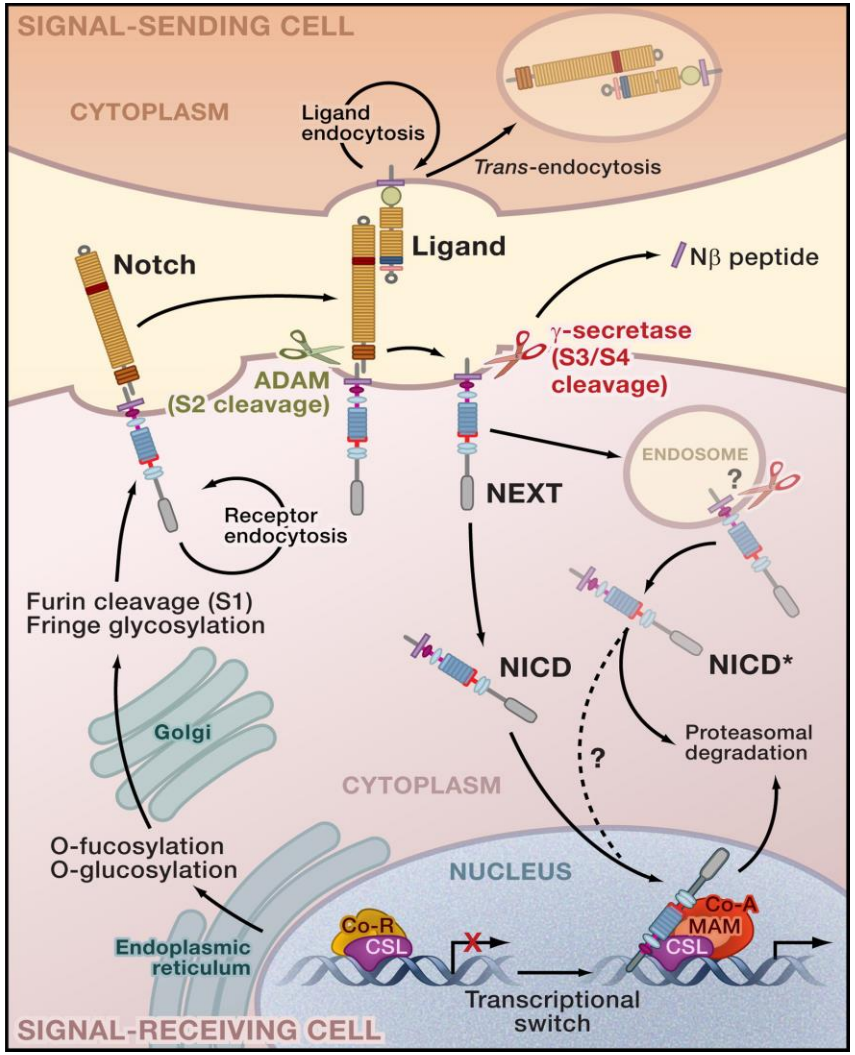
Frequency of Fates for cells at steady state



Errors for Value of A and B at Steady State

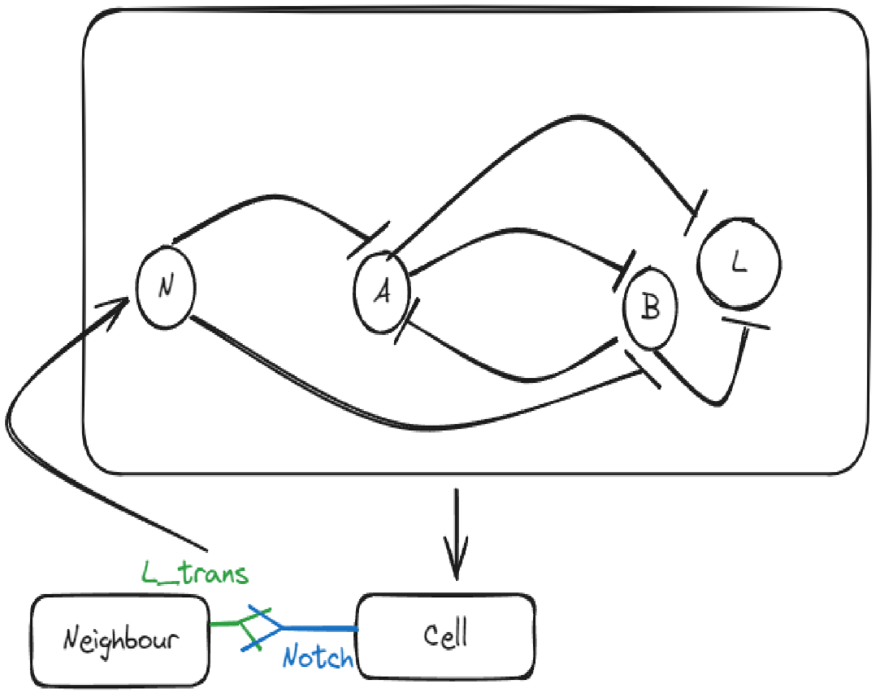


Delta -Notch Signalling Pathway



- Means of interaction between nearest neighbours
- Ligand(Delta) and Receptor(Notch) both are proteins with extracellular domains.
- Notch also has transmembrane and intracellular domain
- Delta binds with Notch, which eventually results in a protease cleaving the transmembrane domain of Notch.
- Notch Intracellular Domain released into the cell
- Moves to the Nucleus where it acts as a co-activator and increases transcription of genes

Toggle switch with Delta-Notch Signalling



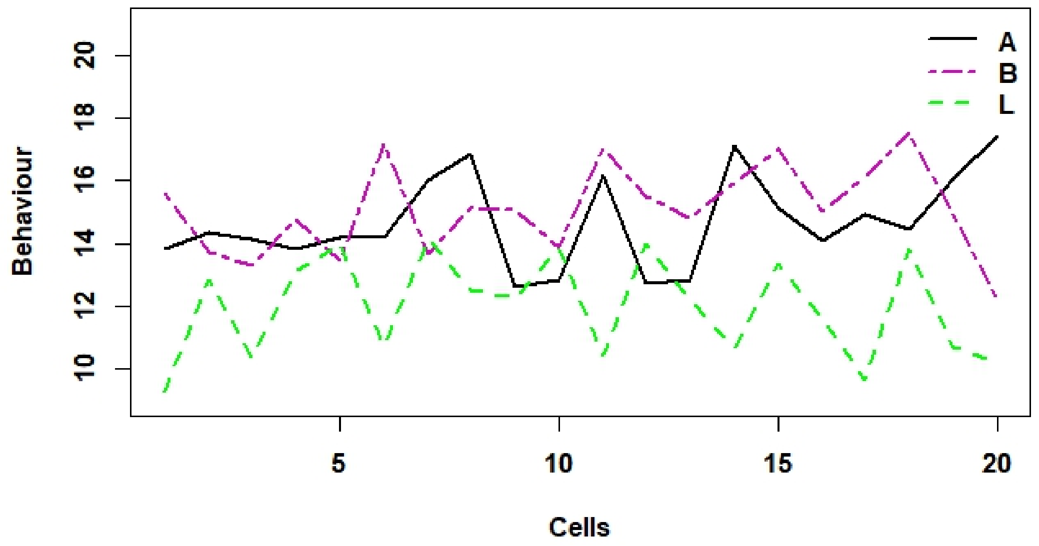
$$\frac{dA[t]}{dt} = \frac{\alpha}{(1 + (B(t)/K) + (N_b[t]))} - \kappa_a A[t]$$

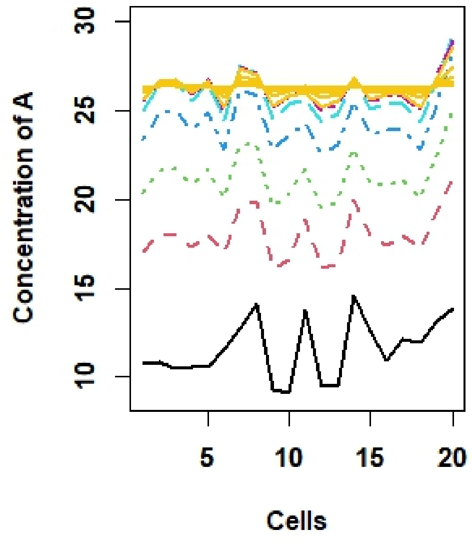
$$\frac{dB[t]}{dt} = \frac{\beta}{(1 + (A(t)/K) + (N_b[t]))} - \kappa_b B[t]$$

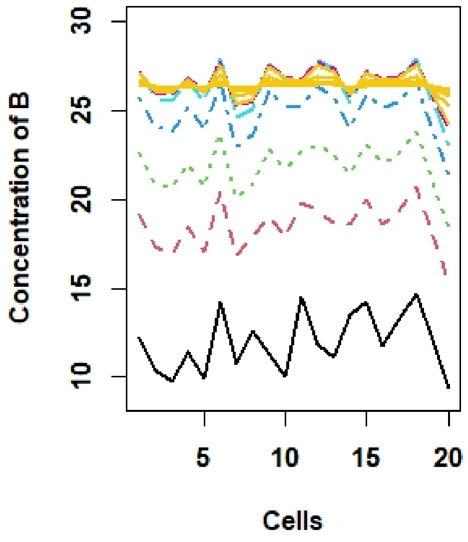
$$\frac{dL[t]}{dt} = \frac{\beta_L}{(1 + (B(t)/K) + (A(t)/K)} - \kappa_L L[t]$$

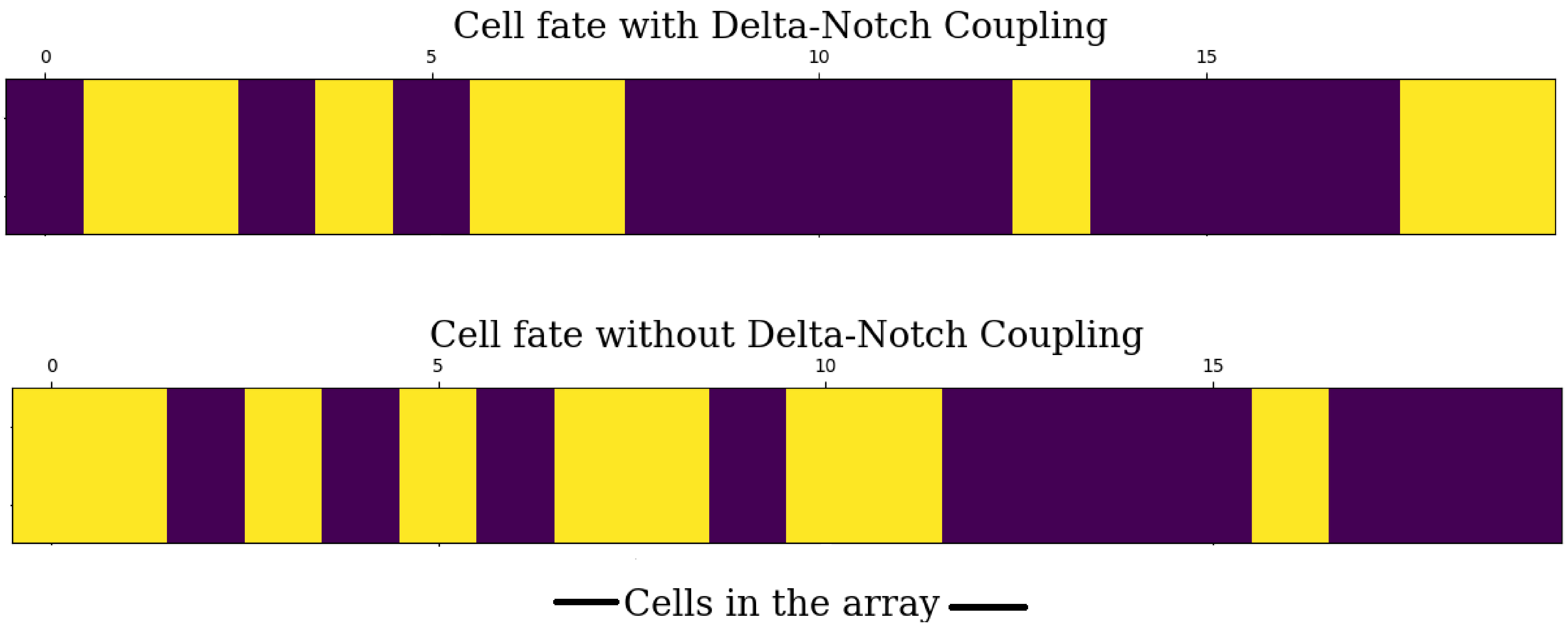
$$\frac{dN_b[t]}{dt} = \frac{\beta_{N_b} L_t[t]}{(K' + L_t[t])} - \kappa_{N_b} N_b[t]$$

Simulation Study

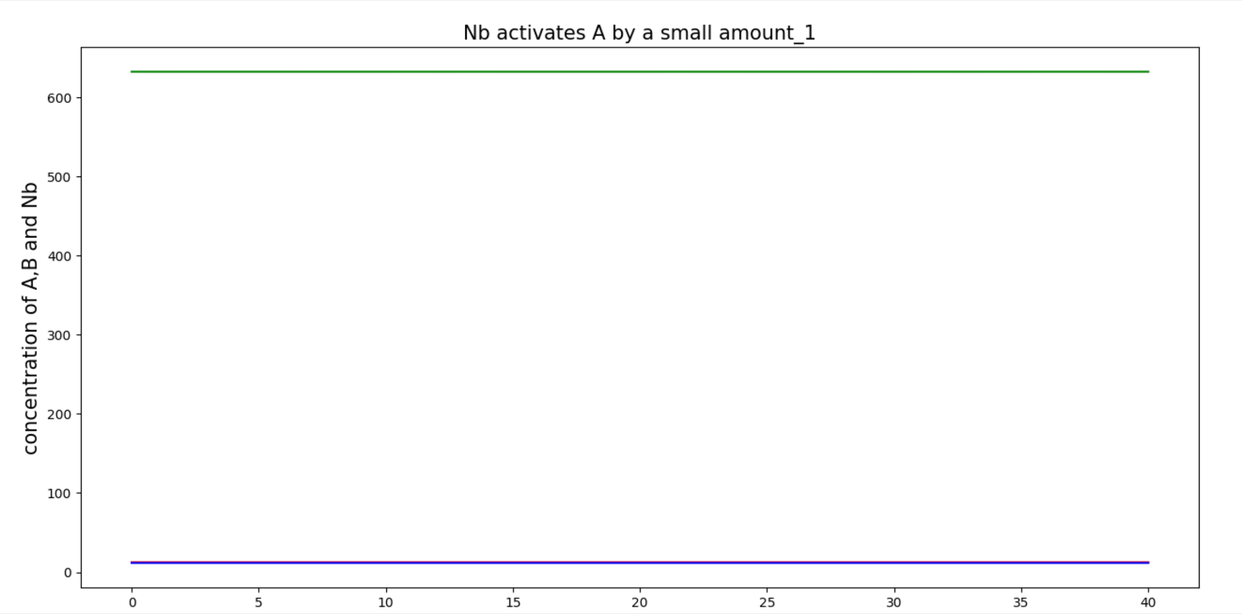




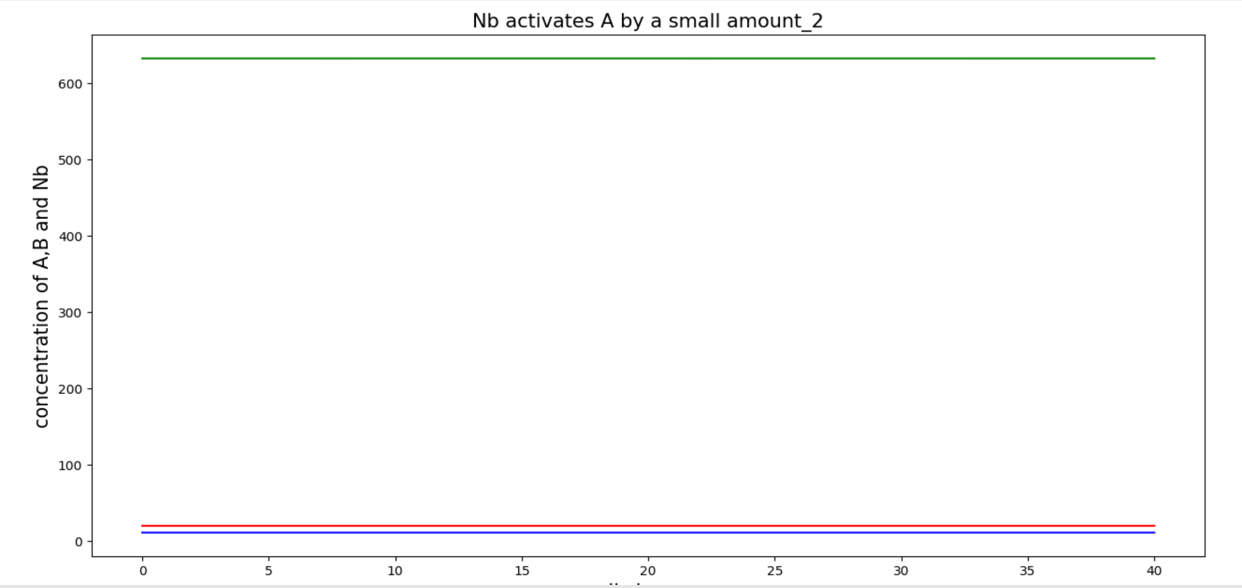


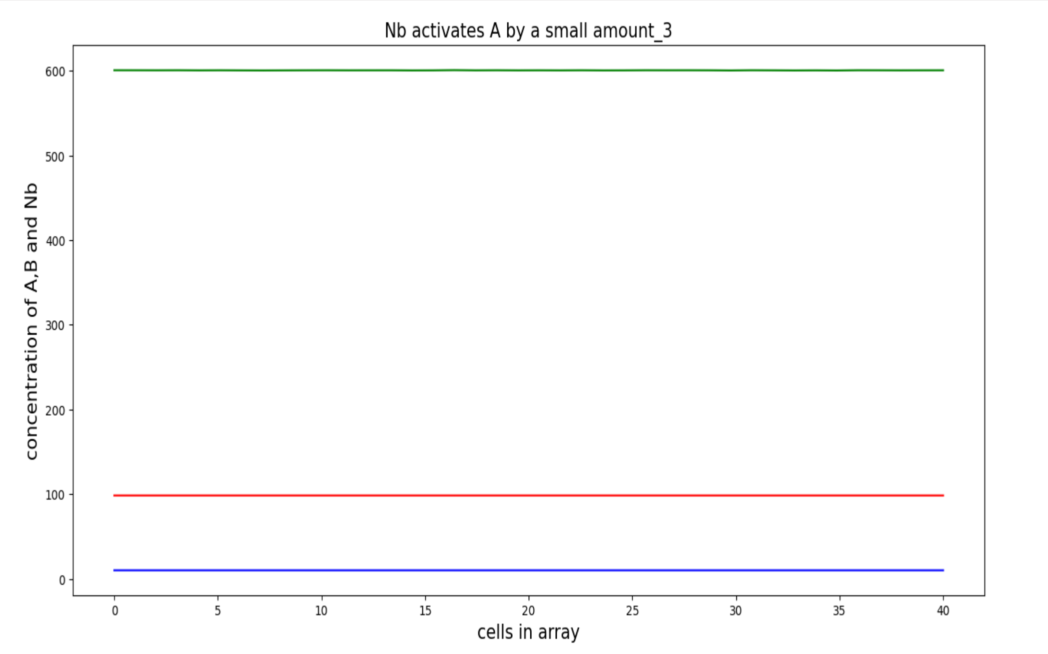


Investigating with and without cell-cell communication



- Nb preferentially activates one of them
- Not useful for patterning





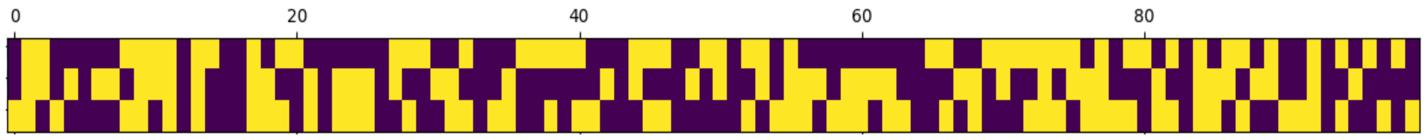
Future Directions

Comprehensively comparing the patterns between coupling(Neighbour interaction) and no interaction cases with same parameter values. Defining relevant metrics for comparisons.

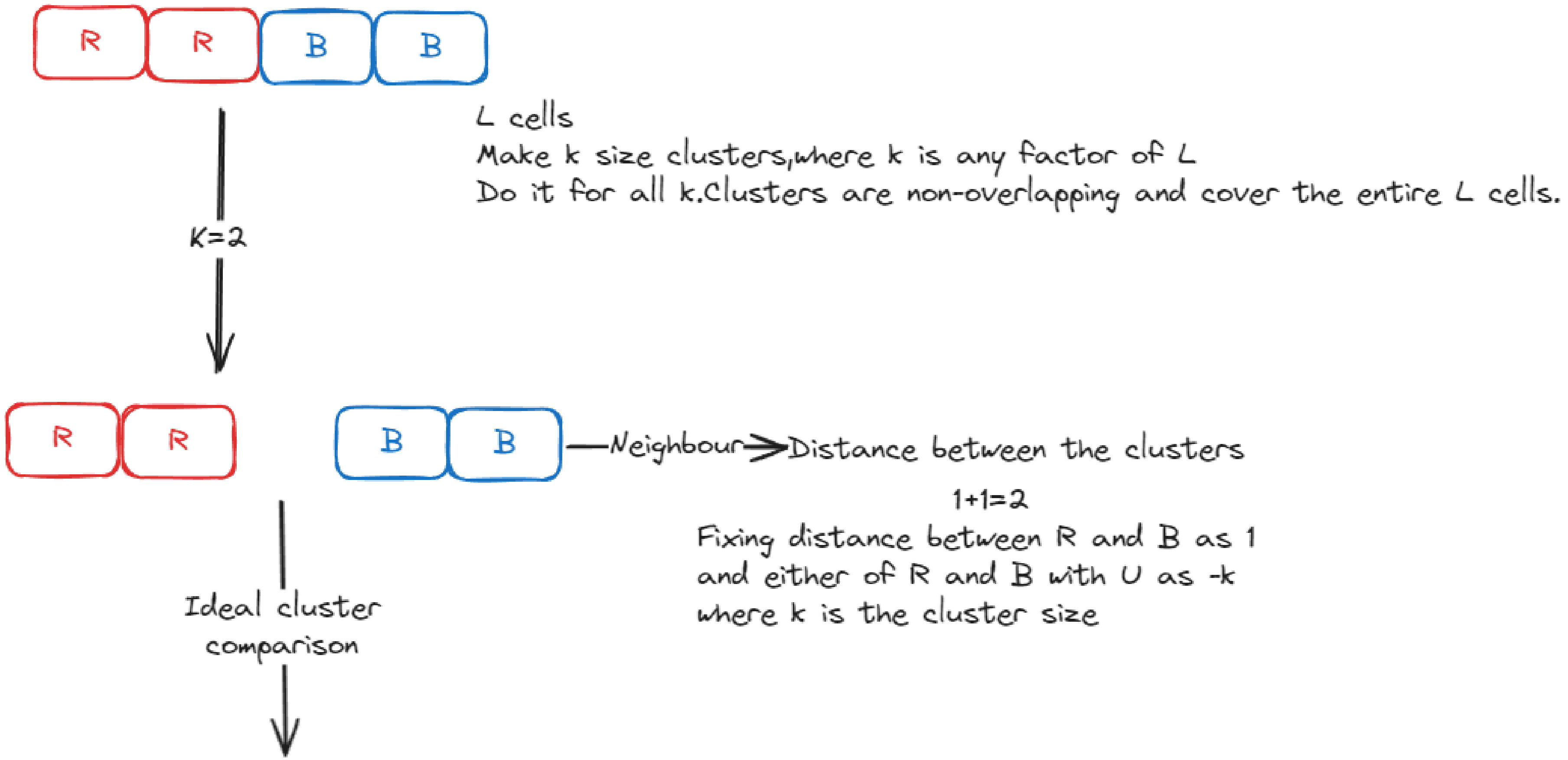
Making varying connections and seeing which motifs give rise to patterns.

Incorporate other kinds of signalling pathways which allow communication over farther distances.

Moving from a 1D array of cells to 2D array.



2D patch of cells without any neighbor interaction



Assuming our ideal clusters are all of same fate R and B
We do comparison with Ideal cluster of either all R or all B.

If the distance between ideal cluster and given cluster is either 0 or k we know that out cells are of same fate.If the distance is k we change it to be 0.

Assuming our ideal pattern is equally sized alternating clusters we would want complete misalignment between neighbors and either complete alignment or misalignment with the ideal cluster.

This would be with a sum of 0 of distance between clusters and ideal cluster and maximum of summation of distance between neighbours.Summation done over all clusters.

References

- C. Kuyyamudi, S.N. Menon and S.Sinha. Flags, Landscapes and Signaling: Contact-mediated inter-cellular interactions enable plasticity in fate determination driven by positional information Indian Journal of Physics, 96(9): 2657-2666 (2022). doi: https://doi.org/10.1007/s12648-022-02348-6

- Raphael Kopan, Ma. Xenia G. Ilagan,The Canonical Notch Signaling Pathway: Unfolding the Activation Mechanism,Cell,Volume 137, Issue 2,2009,Pages 216-233,ISSN 0092-8674. doi: https://doi.org/10.1016/j.cell.2009.03.045.

Code Availability

- All code for our project can be found in the below link:

https://github.com/sidd1729/IMSc-FLS-Workshop-Group-5

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