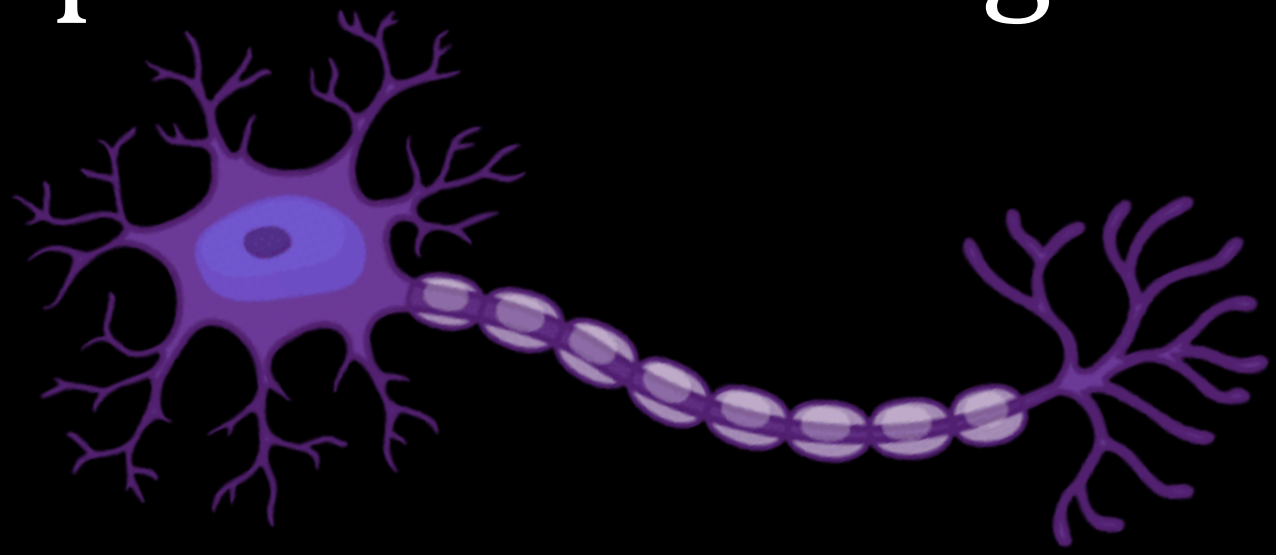
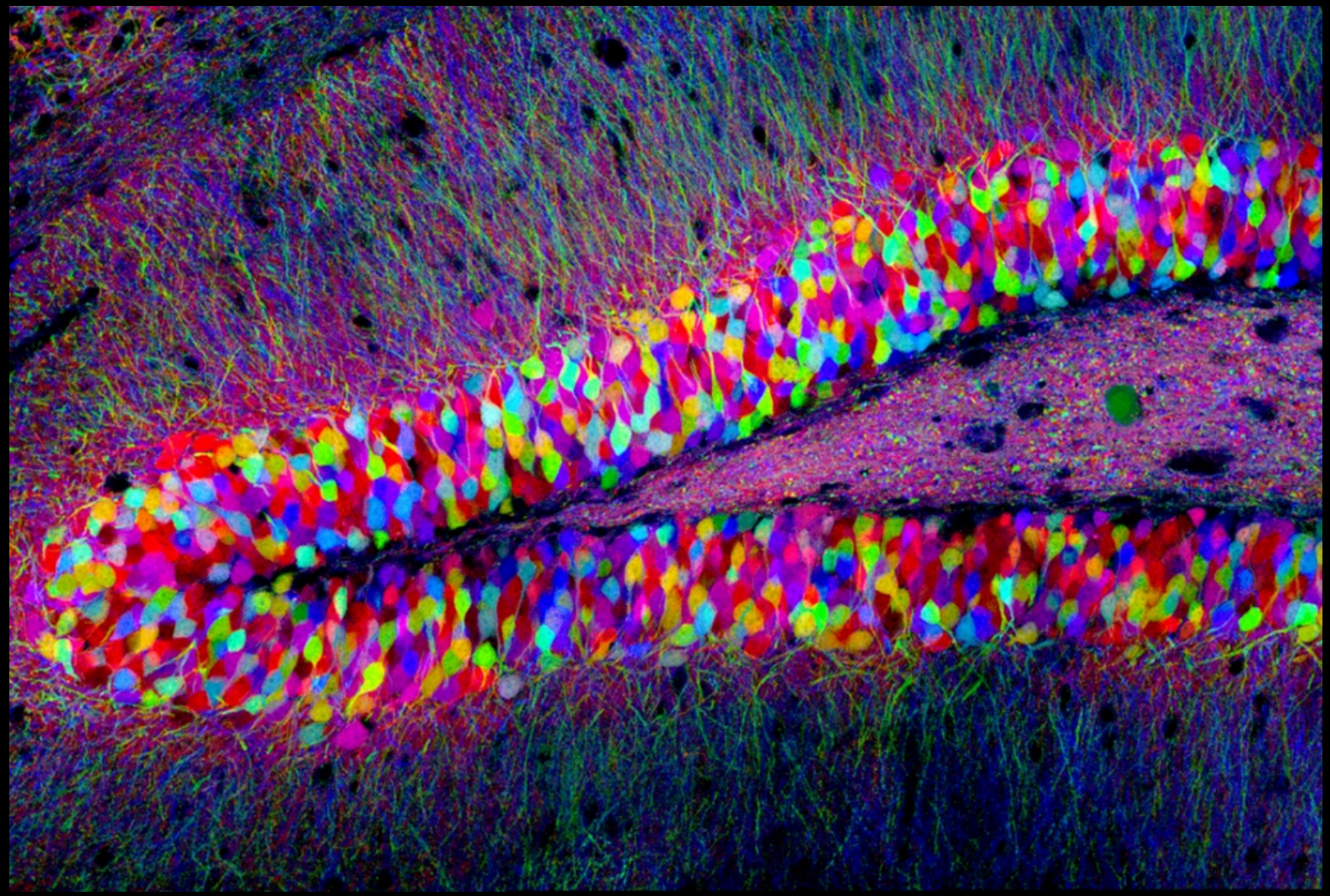
Measuring the Robustness of *Drosophila* Neuroblast Temporal Patterning Network



Aniruddha, Saptarshi and Nimal



Tamily Weissman, Harvard University

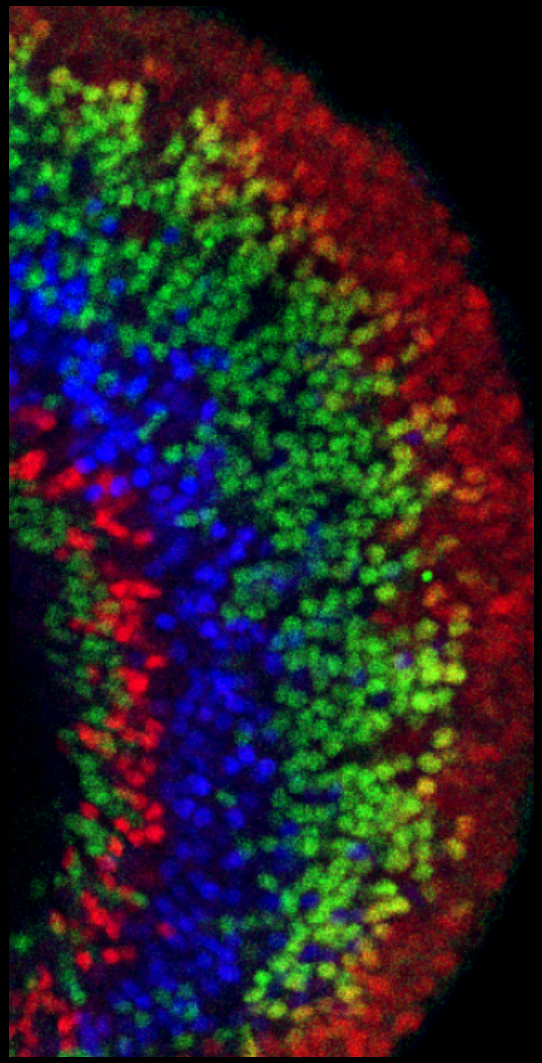
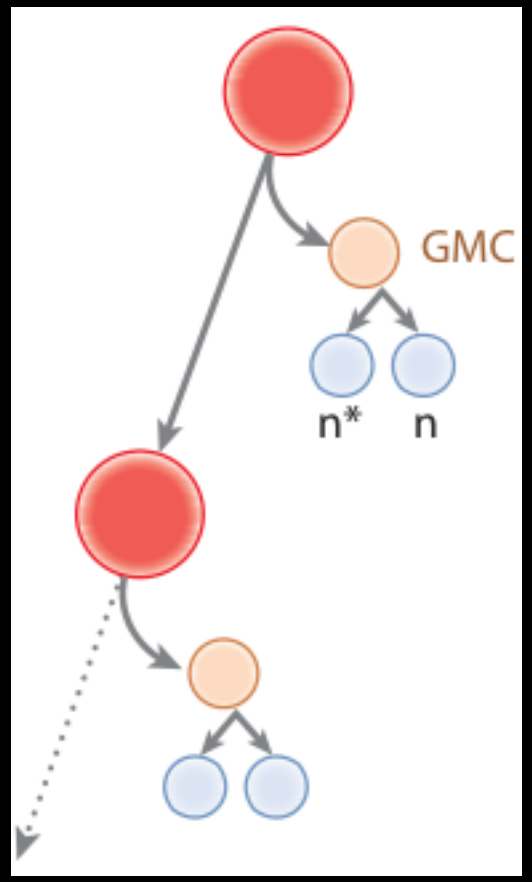


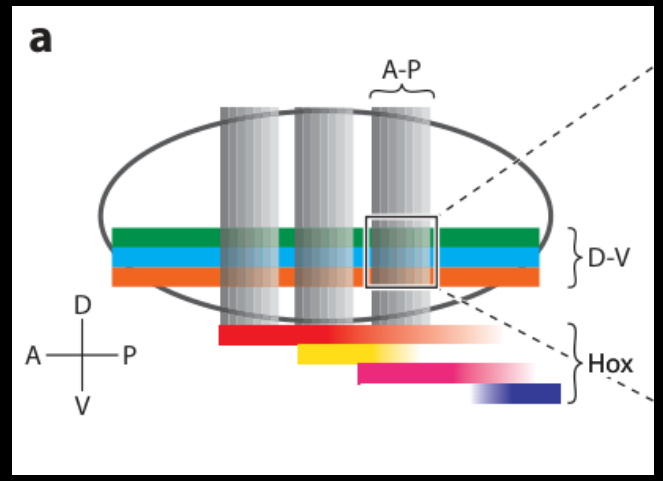
Image Credit: Isabel Holguera

How do you generate such diversity?

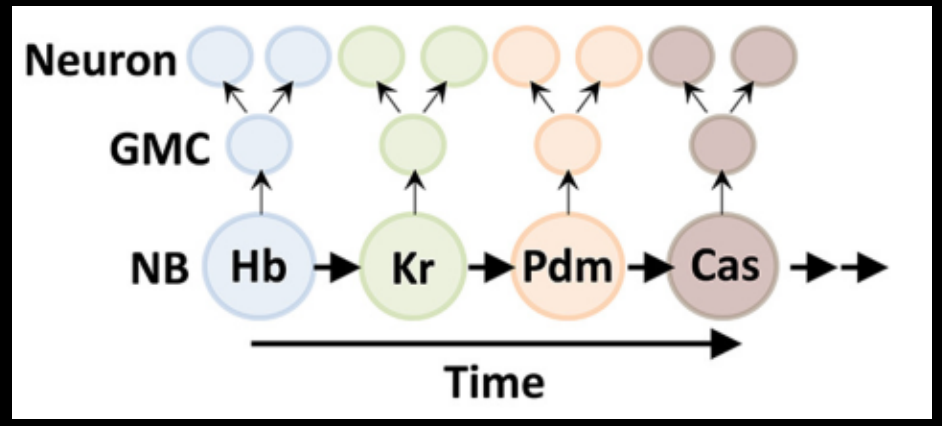
Spatial and Temporal Patterning



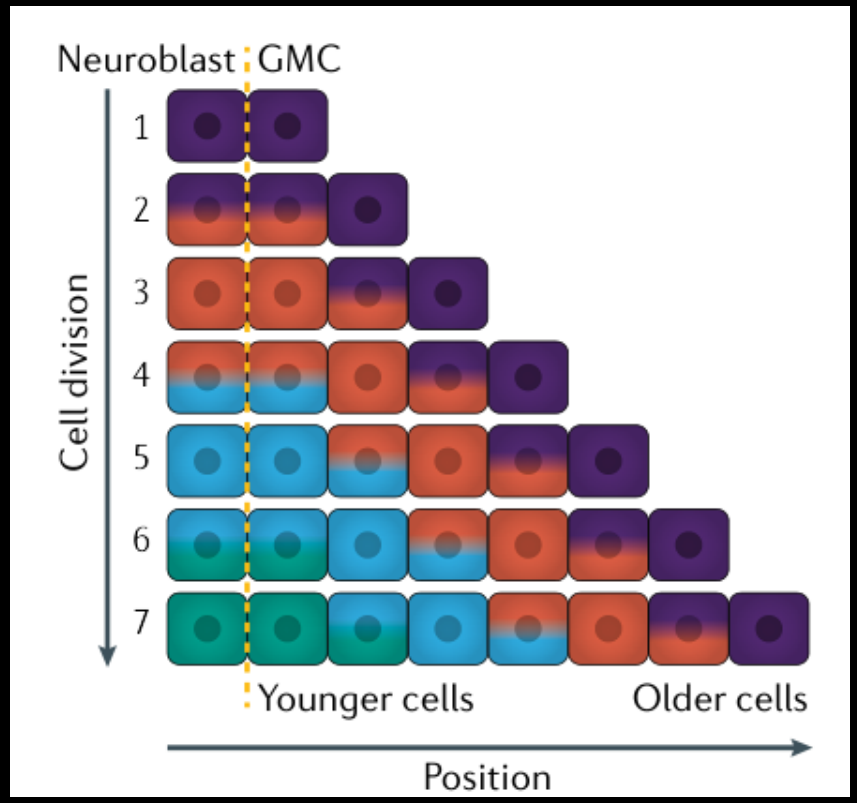
Doe, 2017



Rossi et al., 2021



Averbukh et al., 2018



Negrete Jr and Oates, 2021

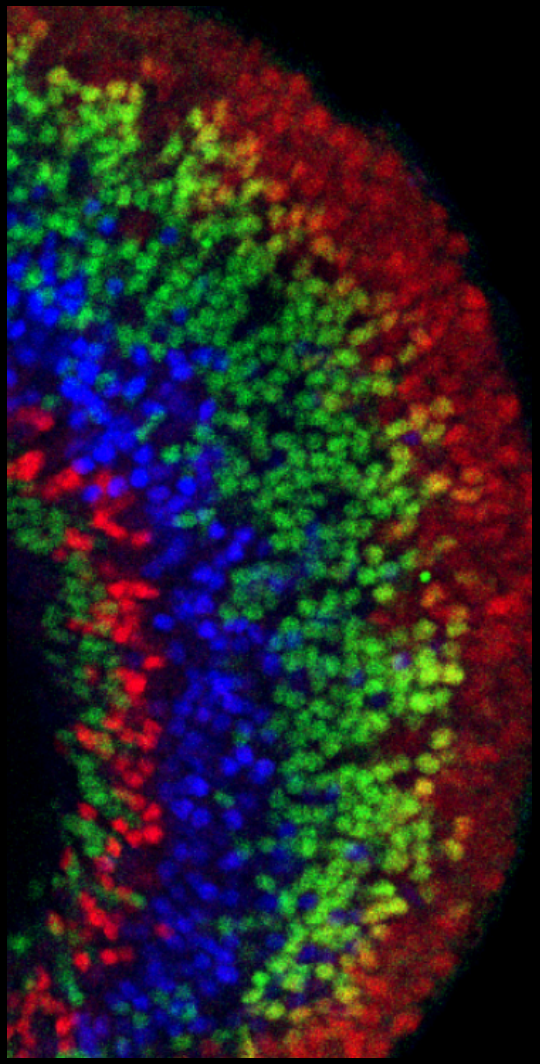


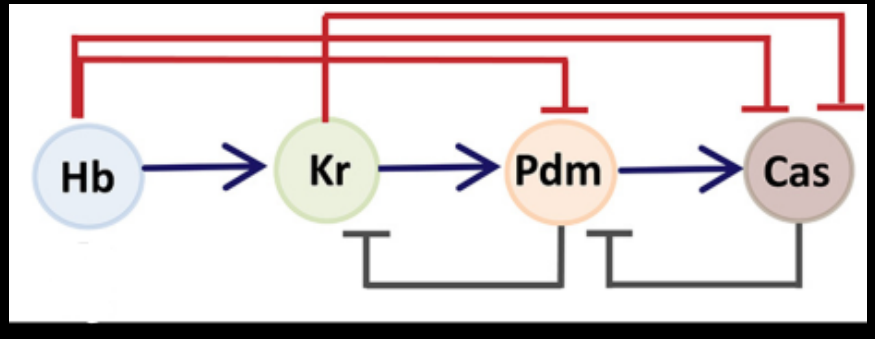
Image Credit: Isabel Holguera

Temporal Patterning

- After formation, each neuroblast (NB) undergoes asymmetric cell divisions every ~45 min to produce a series of ganglion mother cells (GMCs), each of which divides into two post-mitotic neurons.

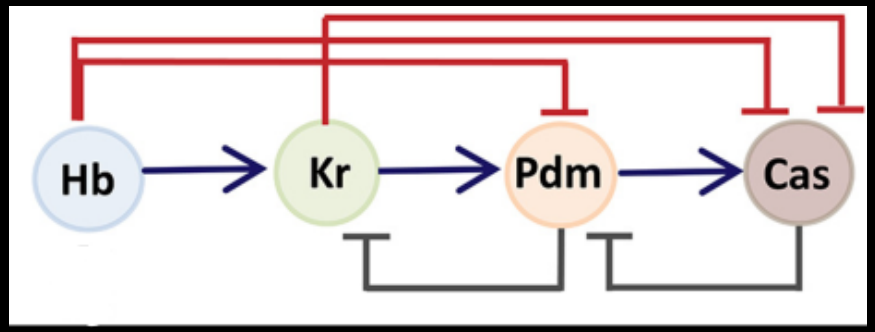
- While progression along the transcription cascade is largely independent of the cell cycle, these two processes must remain synchronized in order to ensure reproducible NB lineage.

- The relay between tTFs is generally thought to be an activator model, in which the preceding factor activates the transcription of the following one. However, mathematical modeling suggests that the timing mechanism may be better described by a repressor-decay model.



Averbukh et al., 2018

Our Question:
Can we measure robustness in terms of the system’s tolerance to gene expression noise?

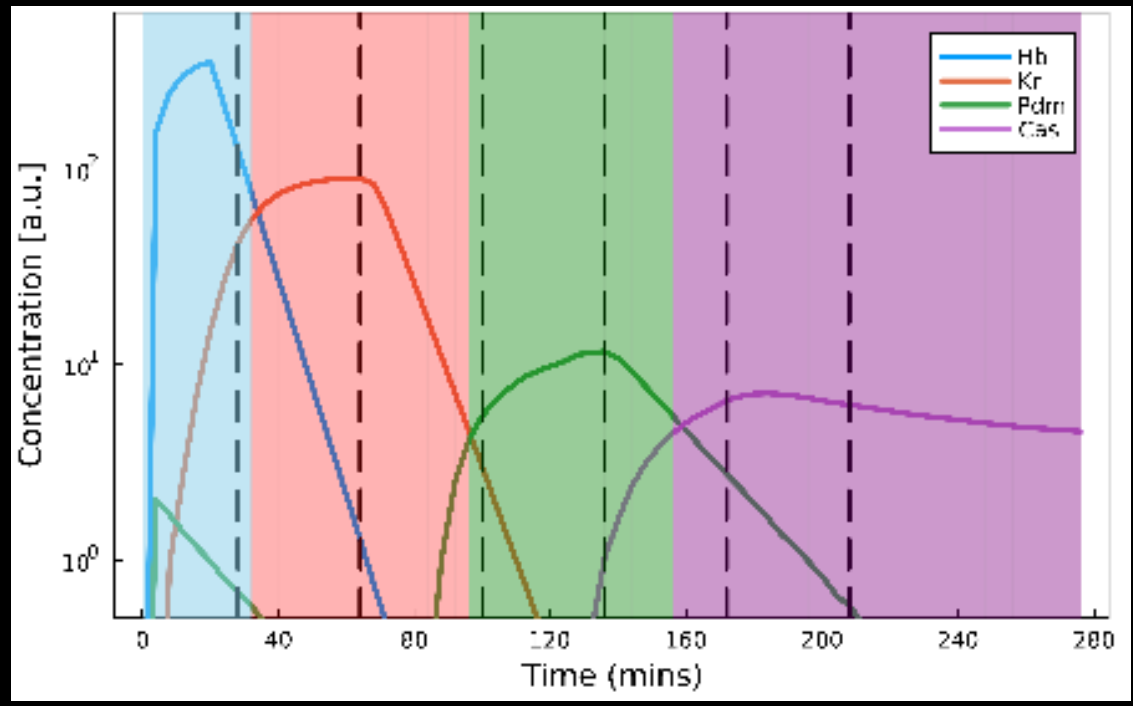


$$(7)\ \frac{d[hb]}{dt} = \theta(t - t_0)\beta_{hb} - \alpha_{hb}[hb]$$

$$(8)\ \frac{d[kr]}{dt} = \beta_{kr}H_A([hb])H_R([pdm]) + \theta(t - t_0)\beta_{kr}^{basal}H_R([pdm]) - \alpha_{kr}[kr]$$

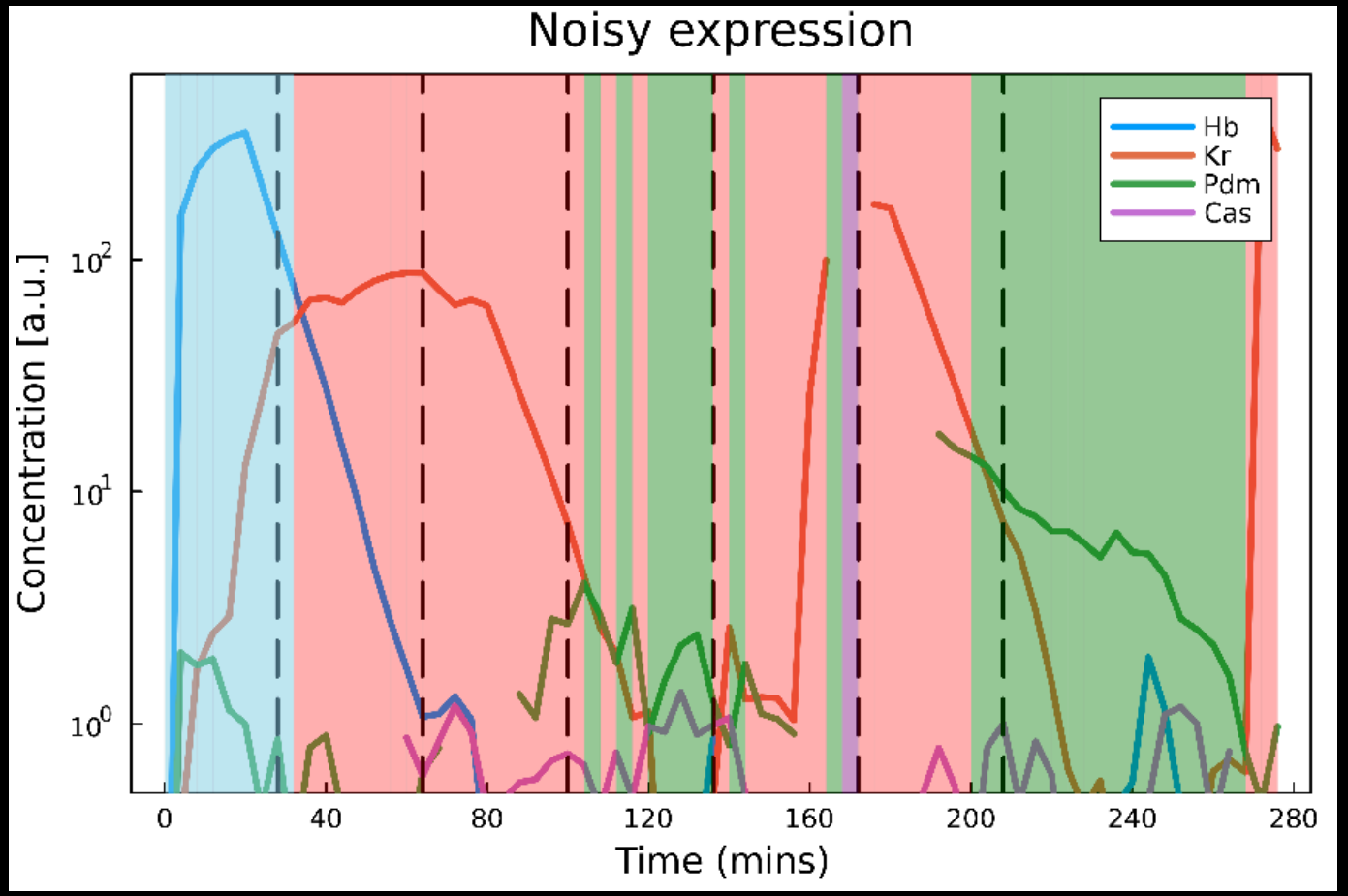
$$(9)\ \frac{d[pdm]}{dt} = \beta_{pdm}H_A([kr])H_R([hb])H_R([cas]) + \beta_{pdm}^{basal}H_R([hb])H_R([cas]) - \alpha_{pdm}[pdm]$$

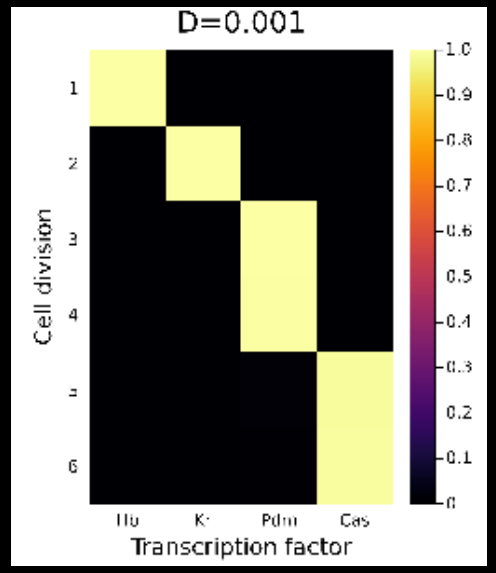
$$(10)\ \frac{d[cas]}{dt} = \beta_{cas}H_A([pdm])H_R([hb])H_R([kr]) + \beta_{cas}^{basal}H_R([hb])H_R([kr]) - \alpha_{cas}[cas]$$

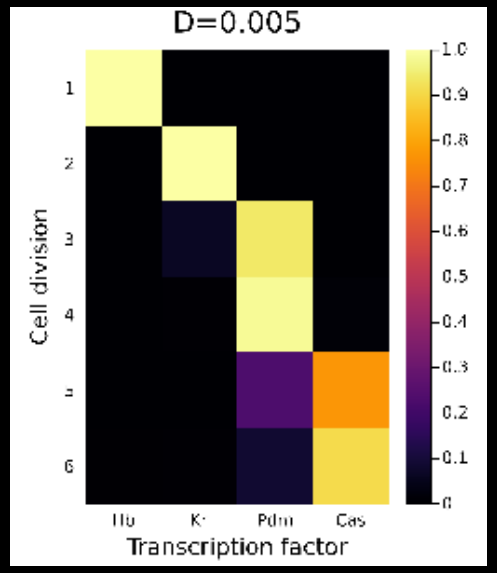


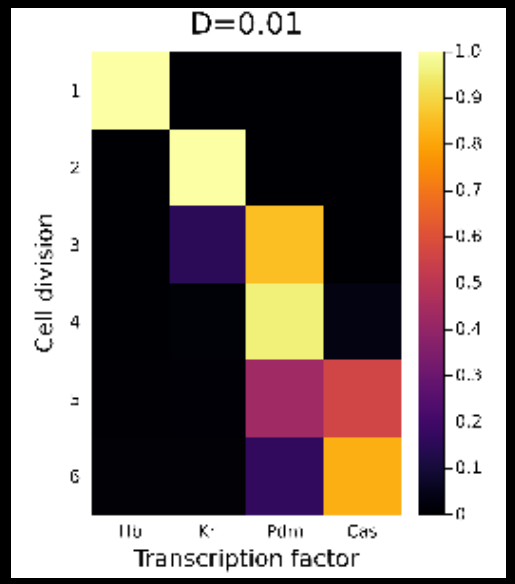
Averbukh et al., 2018

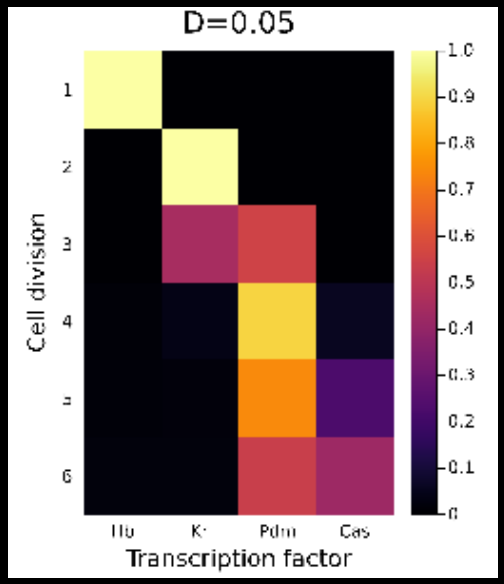
Adding noise:

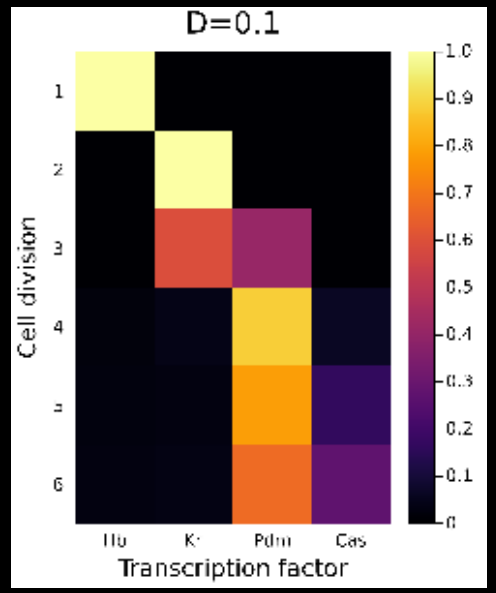


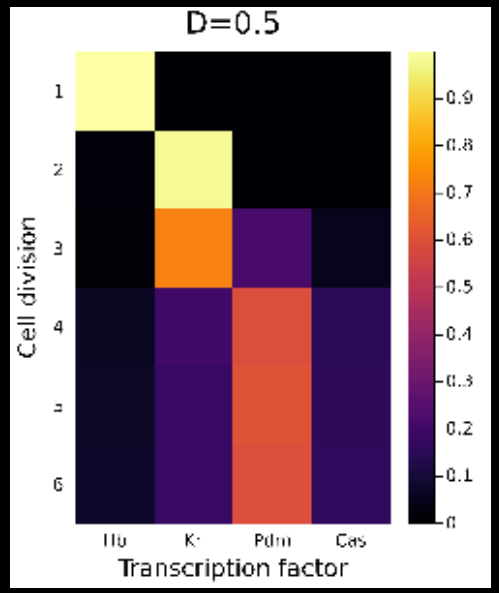

D=0.001
Cell division
Transcription factor
Hb
Kr
Pdm
Cas

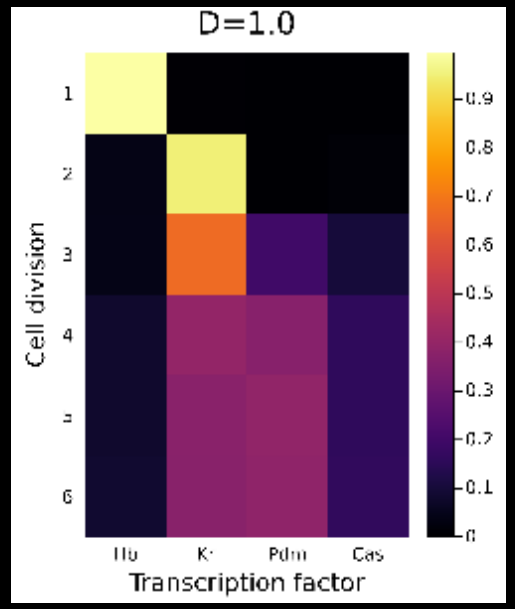

D=0.005
Cell division
Transcription factor
Hb
Kr
Pdm
Cas

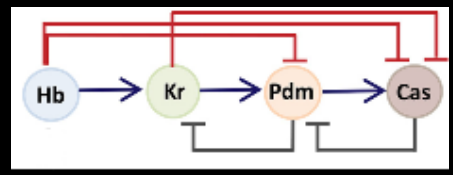

D=0.01
Cell division
Transcription factor
Hb
Kr
Pdm
Cas

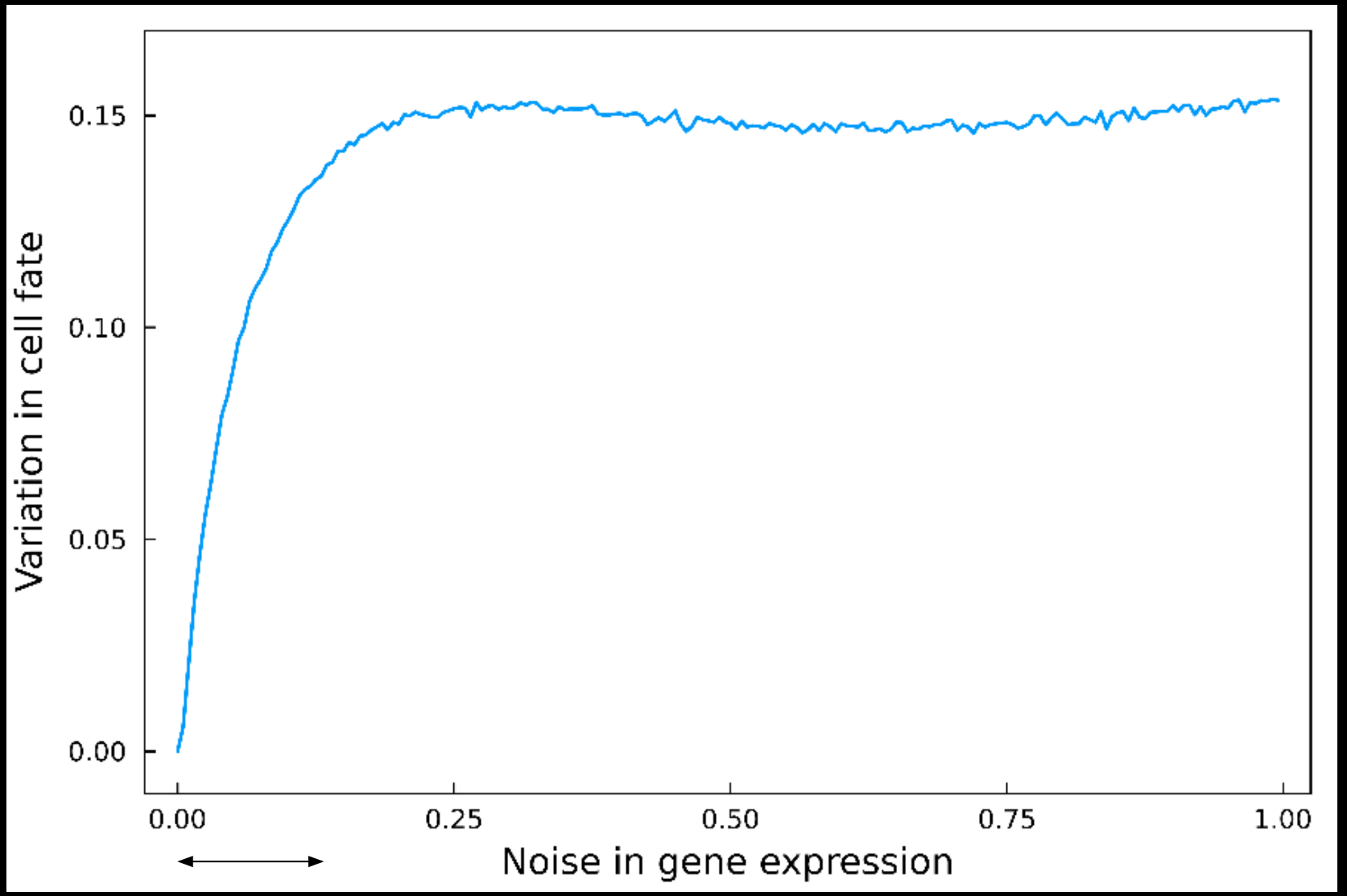

D=0.05
Cell division
Transcription factor
Hb
Kr
Pdm
Cas


D=0.1
Cell division
Transcription factor
Hb
Kr
Pdm
Cas


D=0.5
Cell division
Transcription factor
Hb
Kr
Pdm
Cas

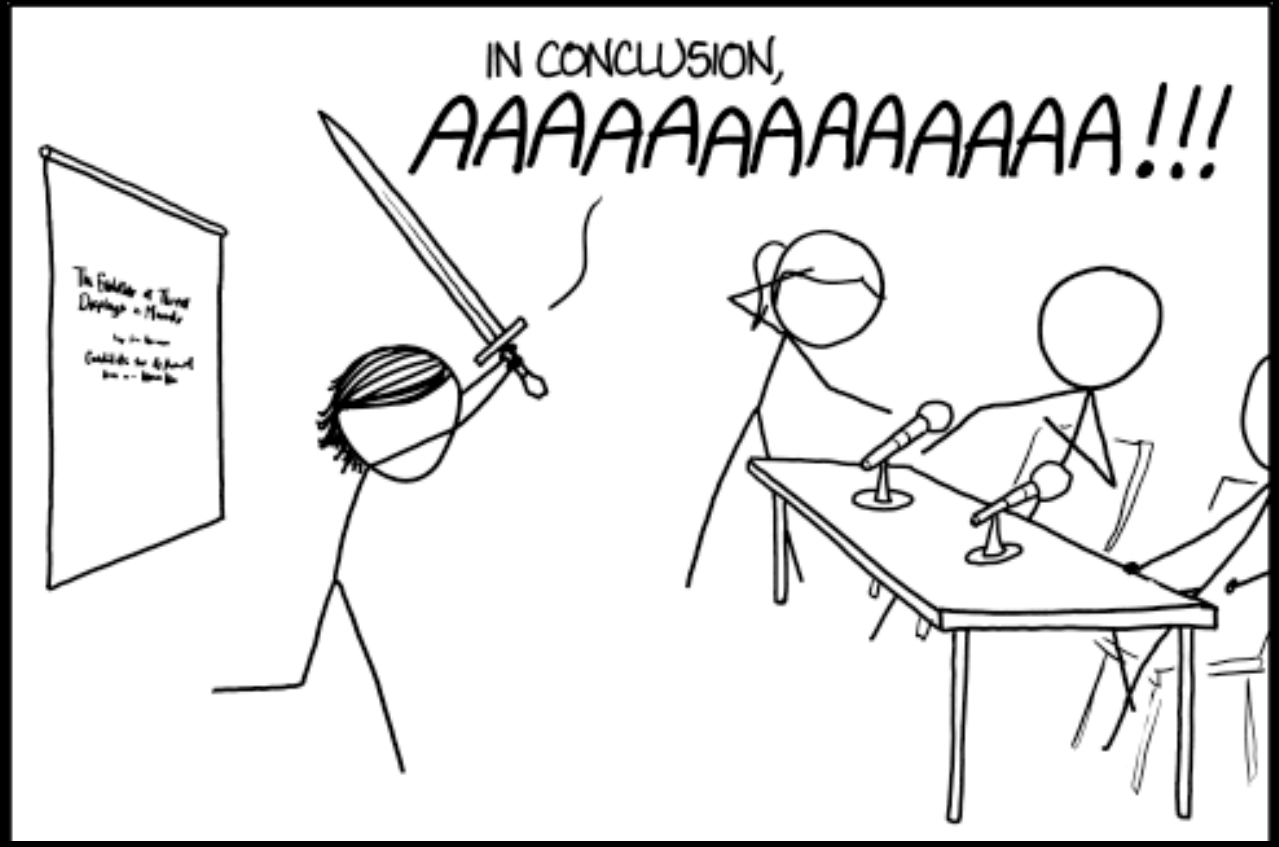

D=1.0
Cell division
Transcription factor
Hb
Kr
Pdm
Cas


Hb
Kr
Pdm
Cas


0.15
0.10
0.05
0.00
Variation in cell fate
0.00
0.25
0.50
0.75
1.00
Noise in gene expression

Future Directions:

- How is patterning maintained in synchrony with the cell division cycle?
- Narrowing down the parameter space based on our robustness measures and making predictions that can be addressed through experiments.



xkcd

Questions? :)