Transcriptional Regulation by the Numbers

4D Advanced Microscopy of Brain Circuits
Cells make decisions about their diet

- Lactose
- Glucose
- Machinery to eat lactose

Graph showing:
- Optical density on the y-axis
- Hours on the x-axis
- 43.5 lactose
- 13.5 glucose

Image showing:
- 0 min
Can the input-output function of regulatory decisions be modeled?

- Can model and experiment agree on the input-output relations of genetic circuits?
The molecular machines that link the “two great polymer languages”
mRNA distributions are the result of production and degradation.

\[
mRNA(t + \Delta t) = mRNA(t) + r \Delta t - \gamma mRNA(t) \Delta t
\]

Where:
- \( r \) is the rate of mRNA production per cell.
- \( \gamma \) is the degradation rate per cell.
- \( \Delta t \) is the time interval.

The diagrams illustrate the distribution of mRNA molecules over time, showing the increase and decrease due to production and degradation.
Statistical mechanics determines the probability of RNA polymerase binding to the promoter sequence.

RNA polymerase can be specifically or non-specifically bound.

Calculate the probability of binding to the promoter using statistical mechanics.

\[ p_{\text{bound}} = \frac{P}{N_{\text{NS}}} e^{-\beta \Delta \epsilon_{\text{pd}}} \]

Repressors turn genes off by decreasing the rate of mRNA production.

\[
p_{\text{bound}} = \frac{p}{N_{\text{NS}}} e^{-\beta \Delta \varepsilon_{pd}} + \frac{2R}{N_{\text{NS}}} e^{-\beta \Delta \varepsilon_{rd}}
\]

\[
\frac{d \text{ mRNA}}{dt} = \alpha p_{\text{bound}}
\]
Traditionally, Fold-Change Was Measured Using Enzymes

Fold-change(lacZ) =

- The use of enzymes has been superseded by fluorescence
From theory to experiment and back again

Biological phenomenon

Propose a toy model

RNAP

Repressor

Promoter

Test predictions using microscopy

Make predictions

Gene expression = \frac{1}{\frac{1}{1} + \frac{2R}{N_{NS}} e^{-\Delta \varepsilon_{rd}/k_B T}}
Preparing our bacterial samples to perform precision measurements

Rewire *E. coli* to produce a fluorescent protein

Green Fluorescent Protein
Measuring gene expression in single cells

Phase contrast

Fluorescence

Segmentation

Overlay with fluorescence

Obtain the fluorescence per cell