

# Mathematical modeling of gene expression

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## Introduction

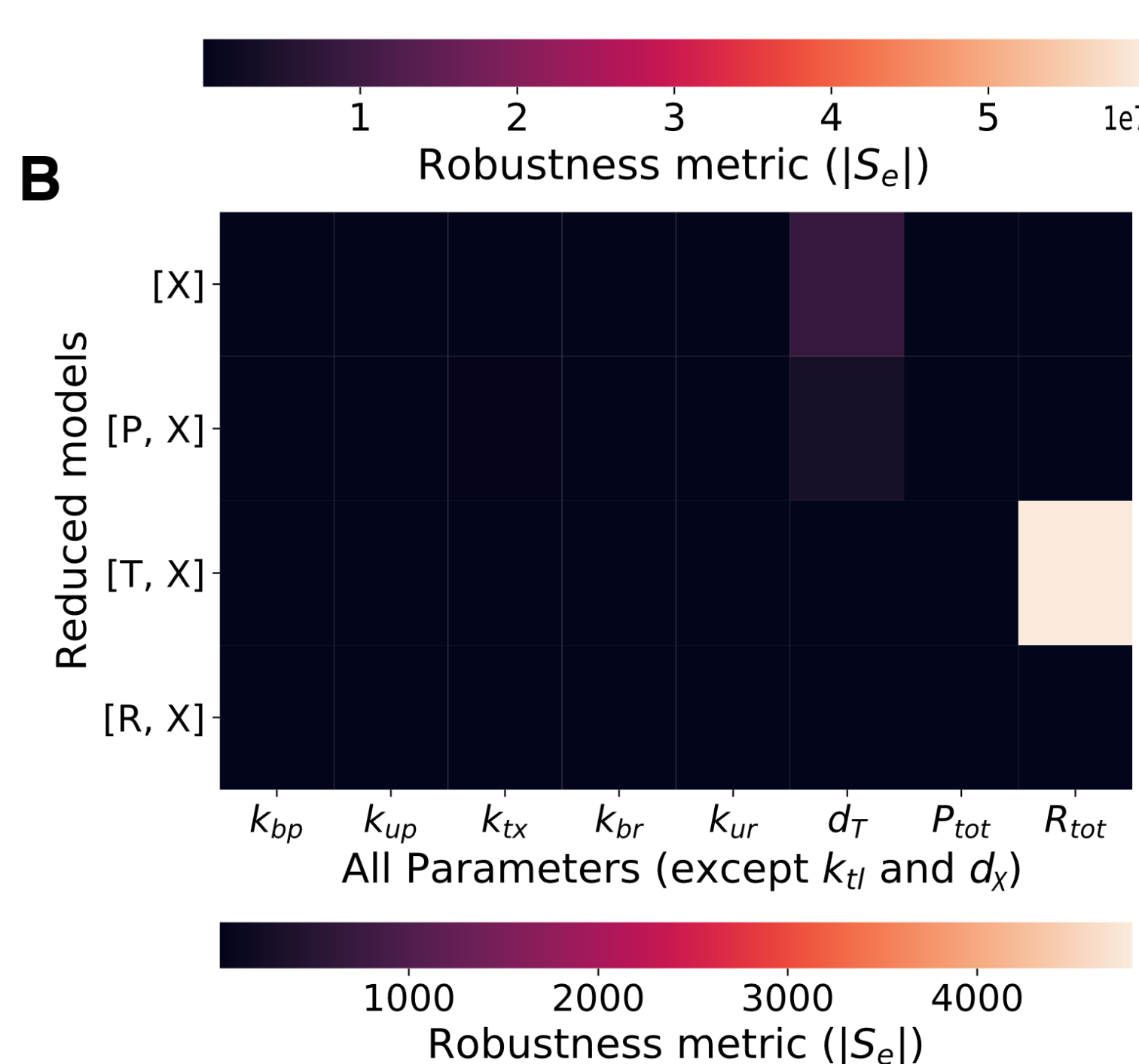
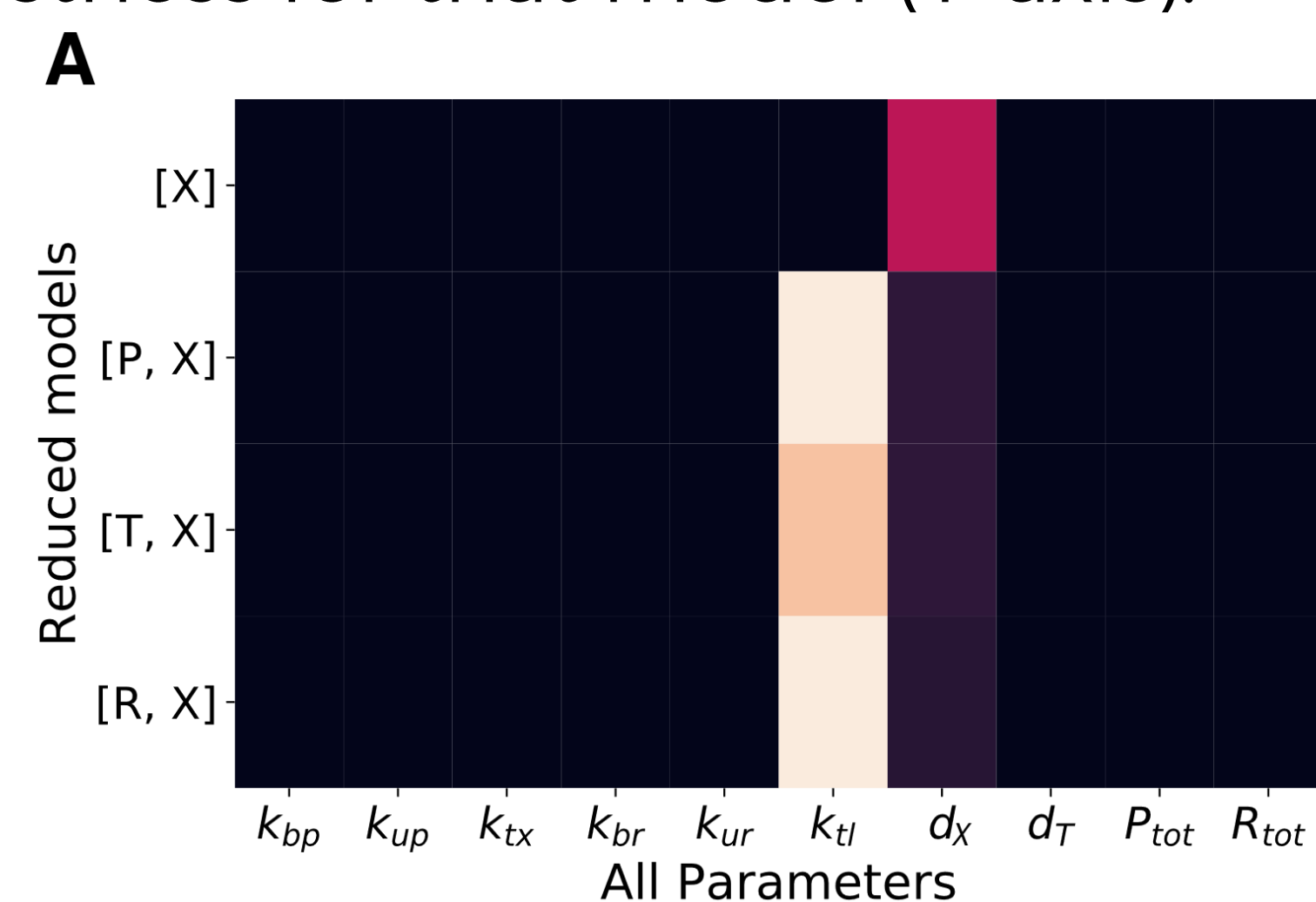
We explore modeling assumptions to validate phenomenological models for gene expression. Both transcription and translation are modeled as two-step processes. With conservation laws and timescale separation assumptions, we derive different possible reduced-order models.

Questions under study:

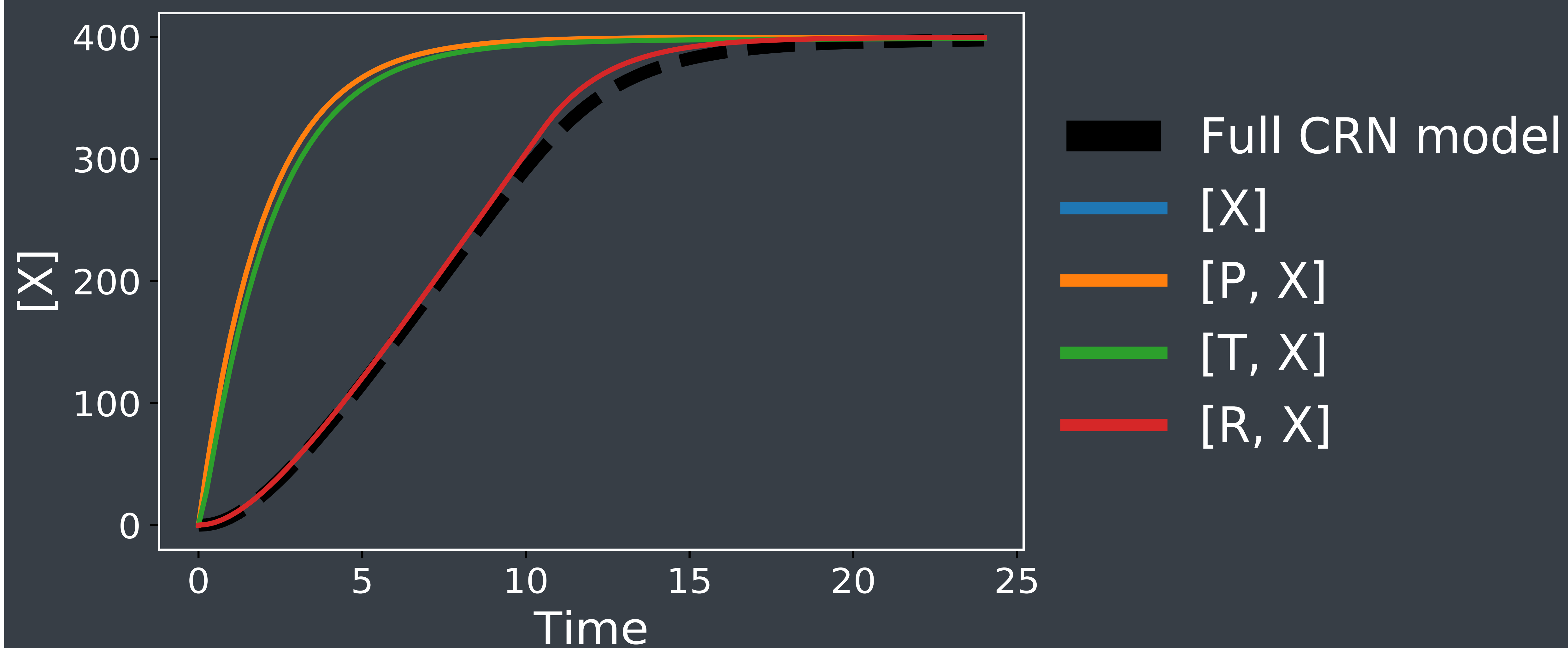
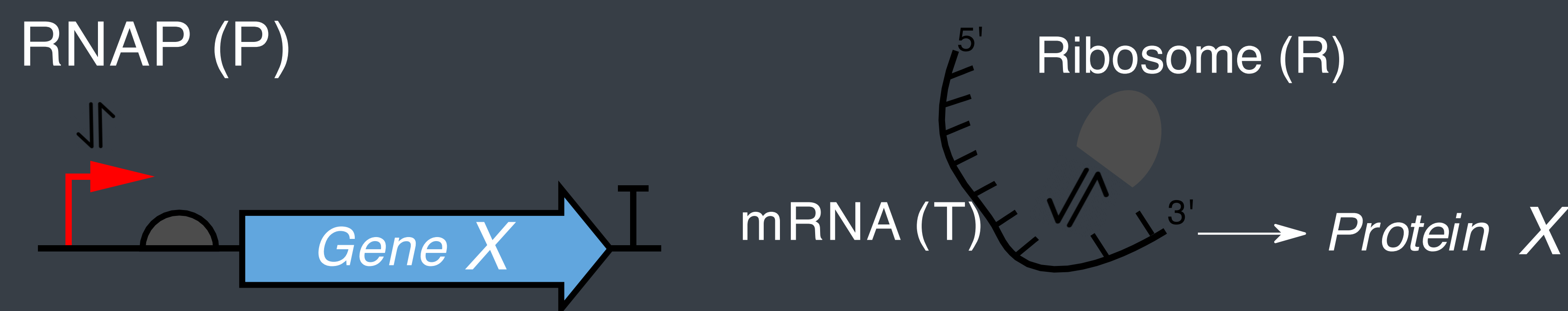
- What are the different operating regimes for the system?
- Which dynamical model accurately describes each behavior?

## Results

Robustness of different gene expression models to parameter perturbations. Key: High value in the heatmap for a parameter entry (X-axis) implies lower robustness for that model (Y-axis).



# A two-state model of free ribosomes and protein concentration captures the details of gene expression dynamics.



## Presenter Notes

The chemical reaction network (CRN) for gene expression and the corresponding ODE model (the full model):

CRN	ODE model
$G + P \xrightleftharpoons[k_{bp}]{k_{up}} C_1$	$\frac{dP}{dt} = (k_{up} + k_{tx}) C_1 - k_{bp} GP$
$C_1 \xrightarrow{k_{tx}} G + P + T$	$\frac{dC_1}{dt} = k_{bp} GP - (k_{up} + k_{tx}) C_1$
$T + R \xrightleftharpoons[k_{br}]{k_{ur}} C_2$	$\frac{dT}{dt} = k_{tx} C_1 + (k_{ur} + k_{tl}) C_2 - k_{br} TR - d_T T$
$C_2 \xrightarrow{k_{tl}} T + R + X$	$\frac{dR}{dt} = (k_{ur} + k_{tl}) C_2 - k_{br} TR$
$T \xrightarrow{d_T} \emptyset$	$\frac{dC_2}{dt} = k_{br} TR - (k_{ur} + k_{tl}) C_2$
$X \xrightarrow{d_X} \emptyset$	$\frac{dX}{dt} = k_{tl} C_2 - d_X X$

The reduced model with mRNA transcript (T) and protein (X) dynamics:

$$\frac{d\hat{T}}{dt} = k_{tx} P_{tot} \left( \frac{G}{K_1 + G} \right) - d_T \hat{T}$$

$$\frac{d\hat{X}}{dt} = k_{tl} R_{tot} \frac{\hat{T}}{K_0 + \hat{T}} - d_X \hat{X}.$$

The reduced model with free ribosome (R) and protein (X) dynamics:

$$\frac{d\hat{R}}{dt} = \frac{d_T (R_{tot} - \hat{R})}{K_0^{-1} \hat{R} + K_d^{-1}} - k_{tx} P_{tot} \left( \frac{G}{K_1 + G} \right) \left( \frac{\hat{R}}{\hat{R} + \frac{K_0}{K_d}} \right)$$

$$\frac{d\hat{X}}{dt} = k_{tl} (R_{tot} - \hat{R}) - d_X \hat{X}.$$

Define the available free ribosomes in the system as

$$R_{\Delta} = R_{tot} - R$$

The reduced model with free available ribosomes and protein dynamics:

$$\frac{d\hat{R}_{\Delta}}{dt} = k_{tx} P_{tot} \left( \frac{G}{K_1 + G} \right) \left( \frac{R_{tot} - \hat{R}_{\Delta}}{R_{tot} - \hat{R}_{\Delta} + \frac{K_0}{K_d}} \right) - \left( \frac{d_T}{K_0^{-1} (R_{tot} - \hat{R}_{\Delta}) + K_d^{-1}} \right) \hat{R}_{\Delta}$$

$$\frac{d\hat{X}}{dt} = k_{tl} \hat{R}_{\Delta} - d_X \hat{X}.$$

## Acknowledgements

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