Modeling I: ODEs and Hill Functions

Section 1: ODEs, Law of mass action and the central dogma

by Alejandro Vignoni (vignoni@isa.upv.es)

An iGEM Engineering Committee Webinar

Webinar 2, May 25th, 2021

sb2cl Lab

Synthetic Biology and Biosystems Control Lab
Valencia UPV

ai2 INSTITUTO DE AUTOMÁTICA E INFORMÁTICA INDUSTRIAL

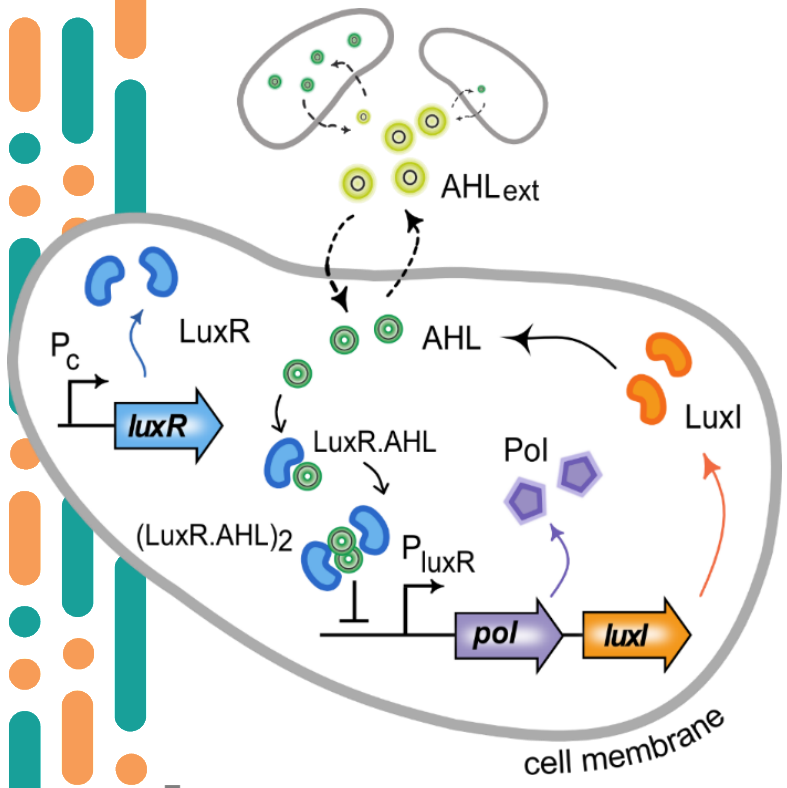
UNIVERSIDAD POLITECNICA DE VALENCIA

Today Webinar's Topics

- Section 1: ODEs, the law of mass action, and the central dogma (~15 min)
- Section 2: Derivation of a Hill function from the law of mass action (~15 min)
- Section 3: Hill function examples and intuitions: effects of parameters on activators, repressors, hybrid promoters, using a Matlab exploration package. (<10min)
- Q&A – (at the end of each 15 minutes block, total 15 min)

Types of models

Schematic → Biochemical Reactions → Mathematical Model (ODEs)



From
Y. Boada (2018)

$$\xrightarrow{C_R} mR$$
$$gPI \xrightarrow{k_{e_I}} gPI + mPI$$
$$mR \xrightarrow{p_R} mR + R$$
$$mPI \xrightarrow{p_I} mPI + PI$$
$$I \xrightarrow{k_A} A + I$$
$$R + A \underset{k_{-1}}{\overset{k_{-1}/k_{d1}}{\rightleftharpoons}} (R \cdot A)$$
$$_2(R \cdot A) \underset{k_{-2}}{\overset{k_{-2}/k_{d2}}{\rightleftharpoons}} (R \cdot A)_2$$
$$gPI + (R \cdot A)_2 \underset{k_{lux}}{\overset{k_{lux}/k_{dlux}}{\rightleftharpoons}} gPI \cdot (R \cdot A)_2$$
$$gPI \cdot (R \cdot A)_2 \xrightarrow{\alpha k_{e_I}} gPI \cdot (R \cdot A)_2 + mPI$$
$$A \underset{DV_c}{\overset{D}{\rightleftharpoons}} A_{ext}$$
$$mPI \xrightarrow{dm_I} \emptyset$$
$$mR \xrightarrow{dm_R} \emptyset$$
$$PI \xrightarrow{d_I} \emptyset$$
$$R \xrightarrow{d_R} \emptyset$$
$$A \xrightarrow{d_A} \emptyset$$

$$\dot{n}_1^i = k_{e_I} n_7^i + \alpha k_{e_I} n_8^i - d_{m_I} n_1^i$$
$$\dot{n}_2^i = C_R - d_{m_R} n_2^i$$
$$\dot{n}_3^i = p_I n_1^i - d_I n_3^i$$
$$\dot{n}_4^i = p_R n_2^i + k_{-1} n_5^i - d_R n_4^i - \frac{k_{-1}}{k_{d1}} n_9^i n_4^i$$
$$\dot{n}_5^i = 2k_{-2} n_6^i + \frac{k_{-1}}{k_{d1}} n_9^i n_4^i + \left(-k_{-1} - d_{RA} - 2\frac{k_{-2}}{k_{d2}} n_5^i\right) n_5^i$$
$$\dot{n}_6^i = k_{lux} n_8^i + \frac{k_{-2}}{k_{d2}} {n_5^i}^2 + \left(-k_{-2} - d_{RA_2} - \frac{k_{lux}}{k_{dlux}} n_7^i\right) n_6^i$$
$$\dot{n}_7^i = k_{lux} n_8^i - \frac{k_{lux}}{k_{dlux}} n_6^i n_7^i$$
$$\dot{n}_8^i = -k_{lux} n_8^i + \frac{k_{lux}}{k_{dlux}} n_6^i n_7^i$$
$$\dot{n}_9^i = D\left(V_c n_{10} - n_9^i\right) - \left(\frac{k_{-1}}{k_{d1}} n_4^i + d_A\right) n_9^i + k_{-1} n_5^i + k_A n_3^i$$
$$\dot{n}_{10} = D\left(-N V_c n_{10} + \sum_{i=1}^{N} n_9^i\right) - d_{A_e} n_{10}$$

But what is an Ordinary Differential Equation (ODE)?

These are equations with **variables** and their **derivatives**

If we have any function (the typical one):

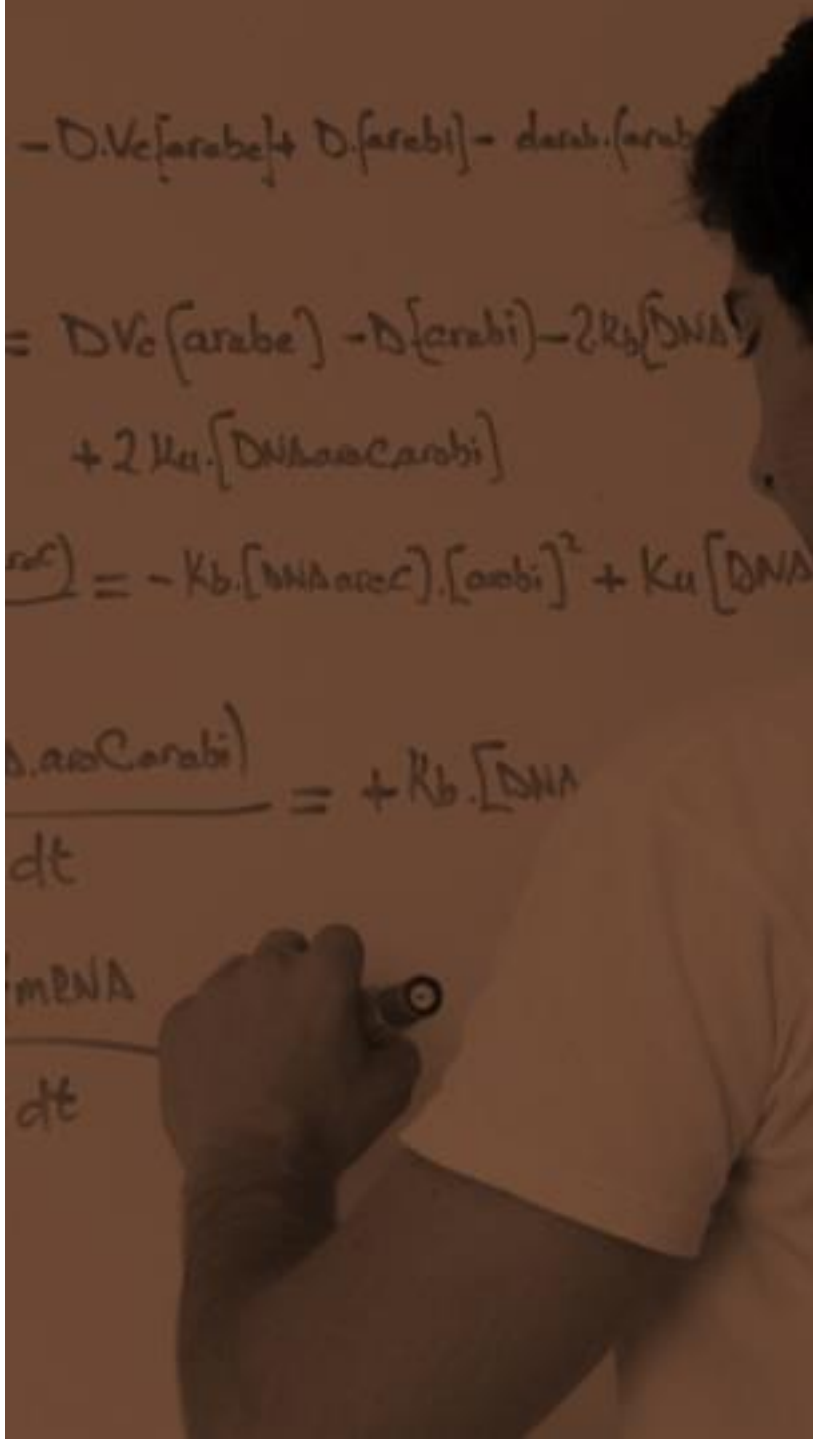
$y = f(t)$ (y only depends on the variable t, but we could have $y = f(t, x_1, x_2, \dots x_n)$)

Do you remember the definition of the derivative of a function?

$$\dot{y} = \frac{df(t)}{dt} = \lim_{h \to 0} \frac{f(t+h) - f(t)}{h}$$

(we can havehigher order derivatives y'', y''', $y^{(n)}$)

But they can be very challenging and difficult!!



Finding a solution…

- **Analytically:** solving for the unknown…

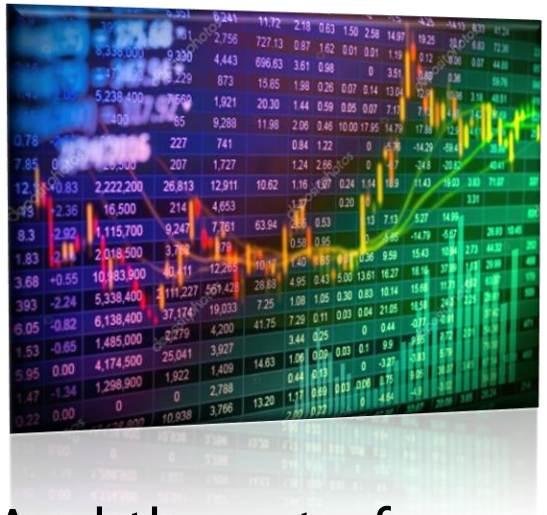
- **Numerically:** in an approximate way.

$$\dot{y} \simeq \frac{f(h+h)-f(x)}{h}$$

(with an h very small)

Why do we use them?

Differential equations describe biological behaviour, physical laws, human activities, and much more....

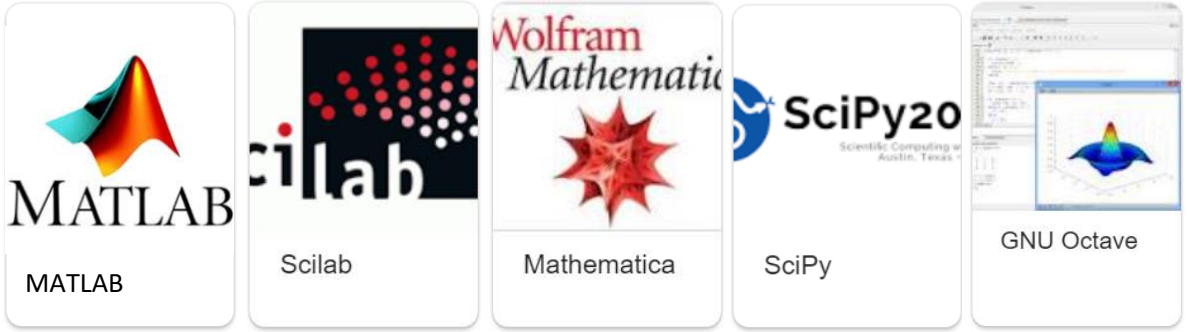


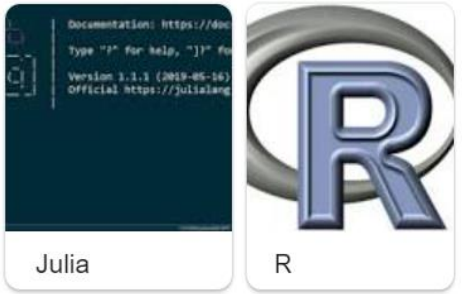
$$\left(-\frac{\partial V}{\partial t}-\frac{1}{2}\sigma^2 S^2\frac{\partial^2 V}{\partial S^2}\right)\Delta t = r\left(-V+S\frac{\partial V}{\partial S}\right)\Delta t$$

$$rV = \frac{\partial V}{\partial t}+\frac{1}{2}\sigma^2 S^2\frac{\partial^2 V}{\partial S^2}+rS\frac{\partial V}{\partial S}.$$

And the set of equations that describe a system or a phenomenon...
is known as ODE model

Software for Ordinary Differential Equations (ODEs) solving





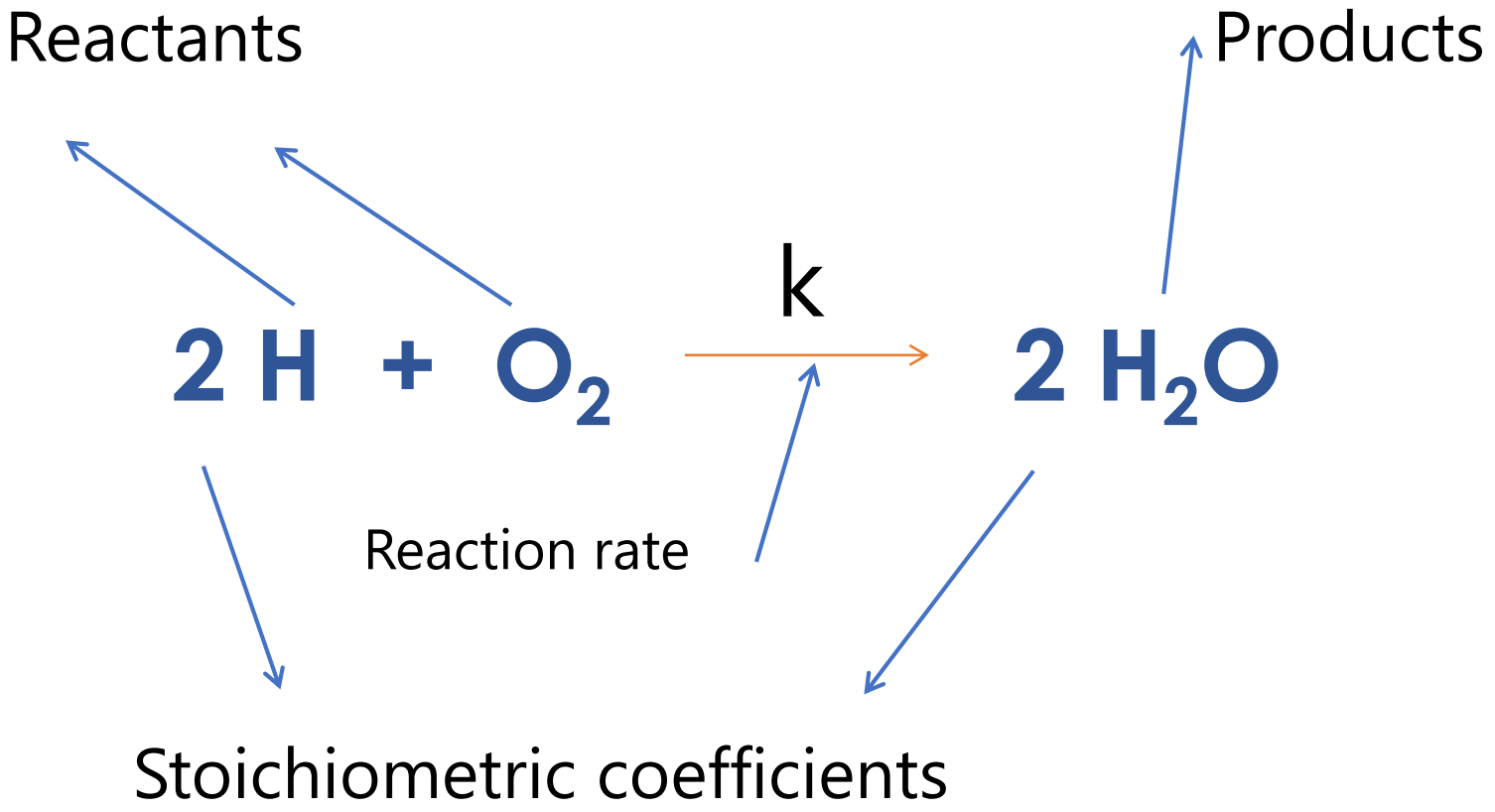
- MATLAB, a technical computing application (MATrix LABoratory)
  FREE LICENSE WITH iGEM
- Maxima, an open-source computer algebra system.
- COPASI, a free software package for the integration and analysis of ODEs.
- GNU Octave, a high-level language, primarily intended for numerical computations.
- Scilab, an open source application for numerical computation.
- Maple, a proprietary application for symbolic calculations.
- Mathematica, a proprietary application primarily intended for symbolic calculations.
- Julia (programming language), a high-level language primarily intended for numerical computations.
- SageMath, an open-source application that uses a Python-like syntax with a wide range of capabilities spanning several branches of mathematics.
- SciPy, a Python package that includes an ODE integration module.
- GNU R, an open source computational environment primarily intended for statistics, which includes packages for ODE solving.

Let us begin this Journey from:

Biochemical Reactions → Mathematical Model (ODEs)

Reminder: Law of mass action and kinetic equations

Example: Reaction of Water



Law of mass action and kinetic equations

Reaction of Water – Kinetics of H_2

Rate of change of $[H]$

Decrease

$$[\dot{H}_2] = -2k[H_2]^2[O_2]$$

Stoichiometric coefficient of $[H_2]$ times the reaction rate k

product of the concentrations of the reactants ($[H_2] \times [H_2] \times [O_2] = [H_2]^2[O_2]$)

Law of mass action and kinetic equations

Reaction of Water – Kinetics of O_2

Rate of change of $[O_2]$

Decrease

$$[\dot{O}_2] = -\ k[H_2]^2[O_2]$$

Stoichiometric coefficient of $[O_2]$ times the reaction rate k

product of the concentrations of the reactants ($[H_2] \times [H_2] \times [O_2] = [H_2]^2[O_2]$)

Law of mass action and kinetic equations

Reaction of Water – Kinetics of O_2

$$2\,H_2 + O_2 \xrightarrow{k} 2\,H_2O$$

Rate of change of $[H_2O]$

Increase

$$[\dot{H_2O}] = +2k[H_2]^2[O_2]$$

Stoichiometric coefficient of $[H_2O]$ times the reaction rate k

product of the concentrations of the reactants ($[H_2] \times [H_2] \times [O_2] = [H_2]^2[O_2]$)

Law of mass action and kinetic equations

Reaction of Water – Kinetics

$$2\,H_2 + O_2 \xrightarrow{k} 2\,H_2O$$

$$[\dot{H}_2] = -2k[H_2]^2[O_2]$$

$$[\dot{O}_2] = -\,k[H_2]^2[O_2]$$

$$[\dot{H_2O}] = 2k[H_2]^2[O_2]$$

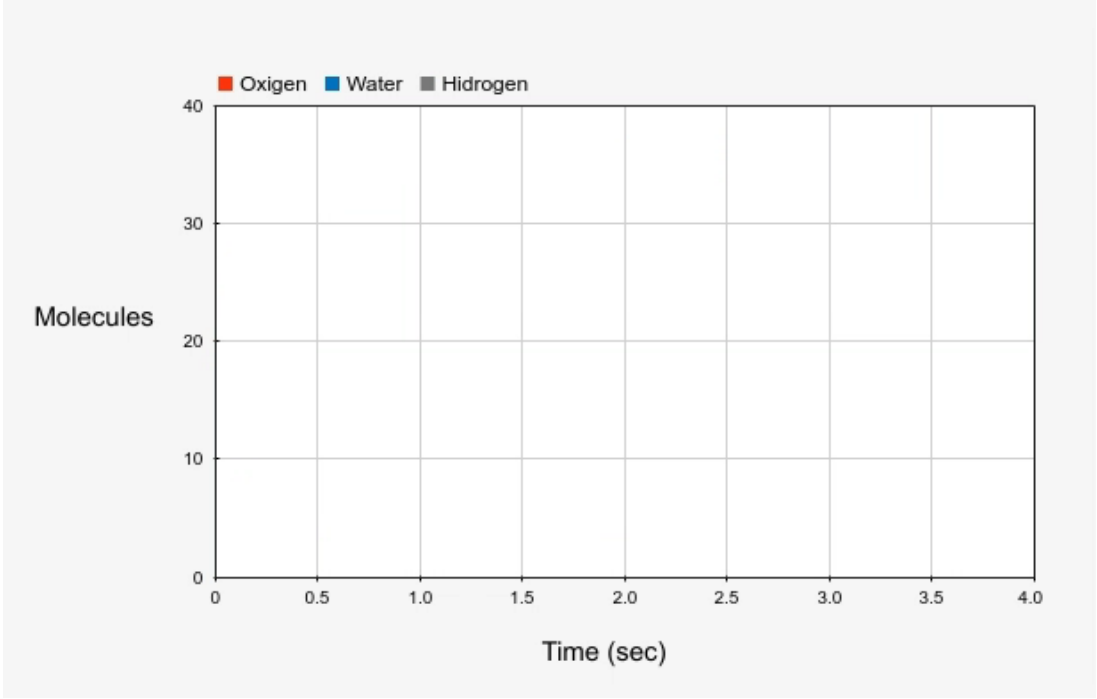
Reaction of Water – Kinetics

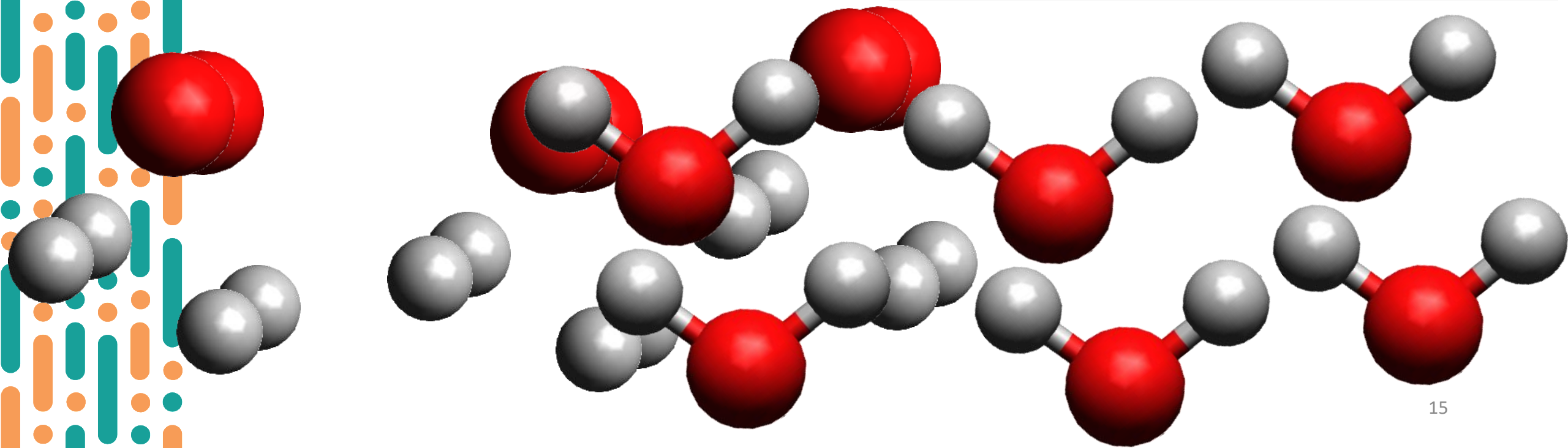
$$2\,H_2 + O_2 \xrightarrow{k} 2\,H_2O$$

$$[\dot{H}_2] = -2k[H_2]^2[O_2]$$

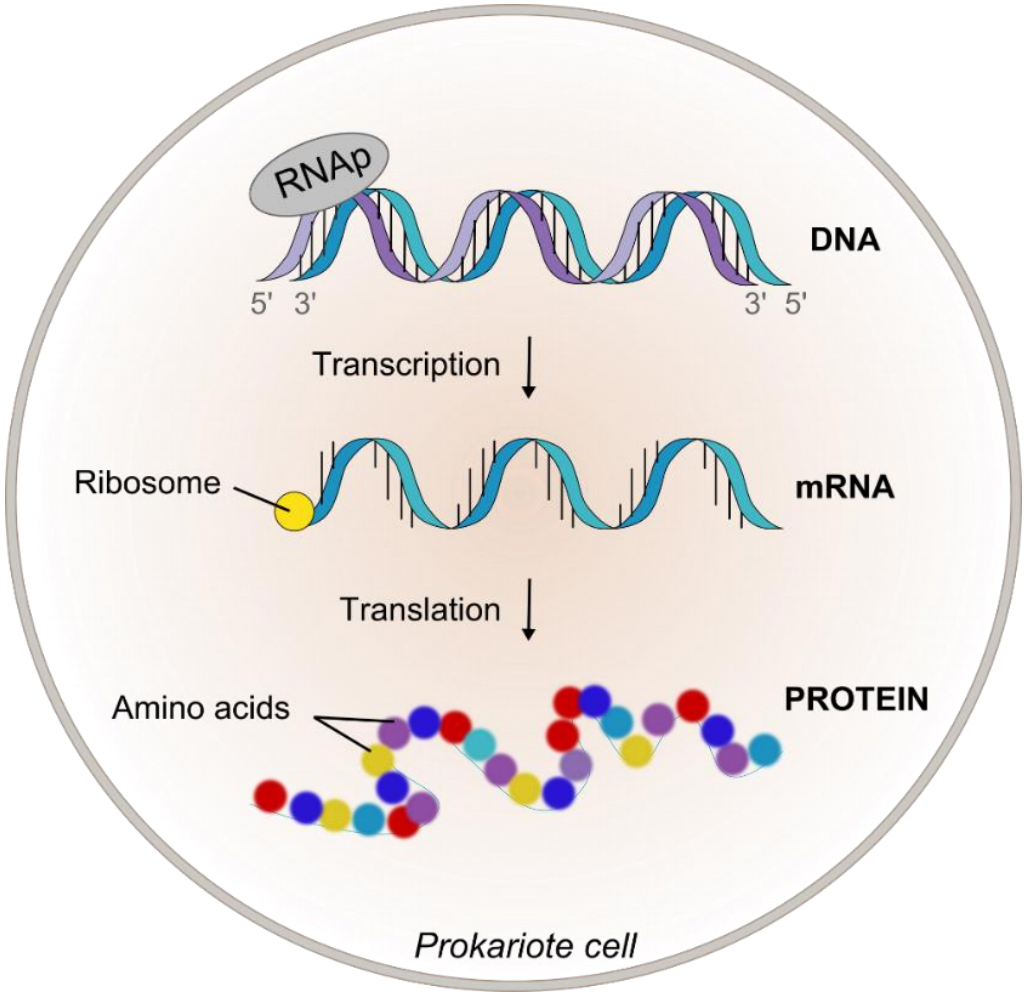
$$[\dot{O}_2] = -\ k[H_2]^2[O_2]$$

$$[\dot{H_2O}] = 2k[H_2]^2[O_2]$$





The central dogma of molecular biology

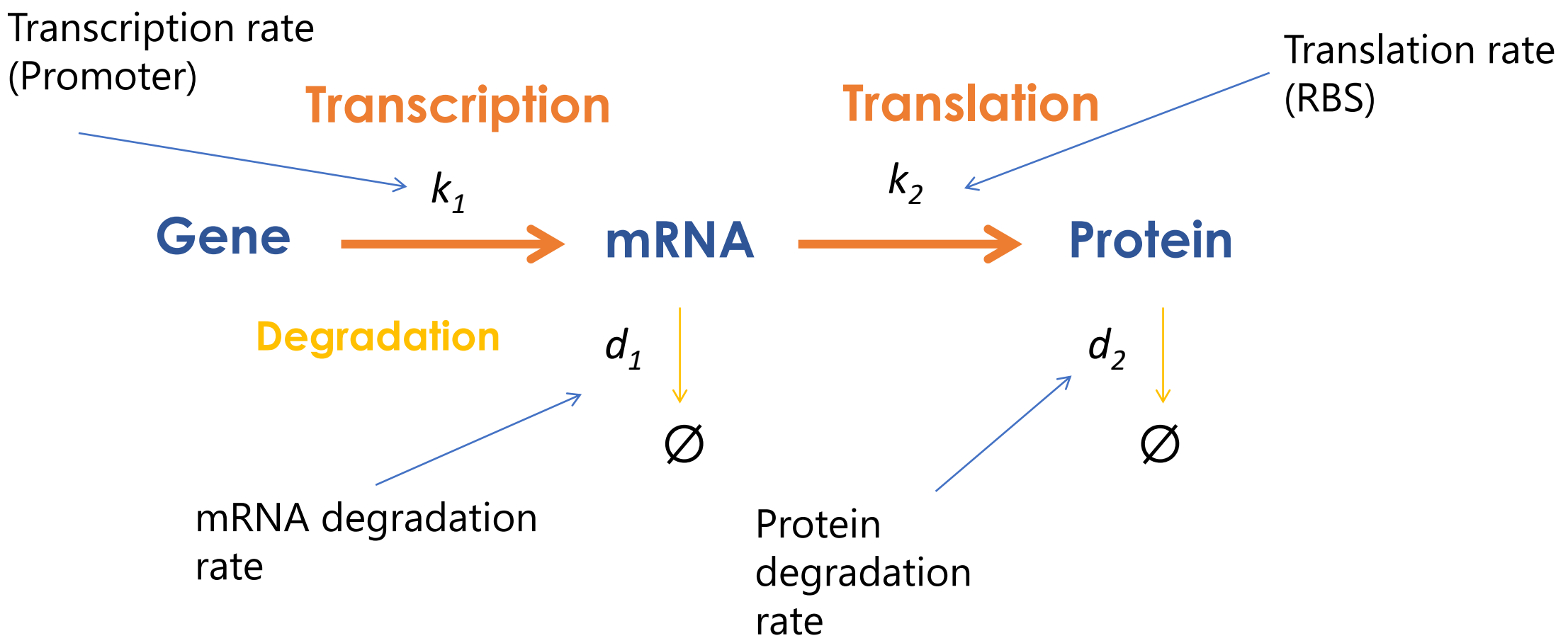


Transcription of DNA by RNA polymerase

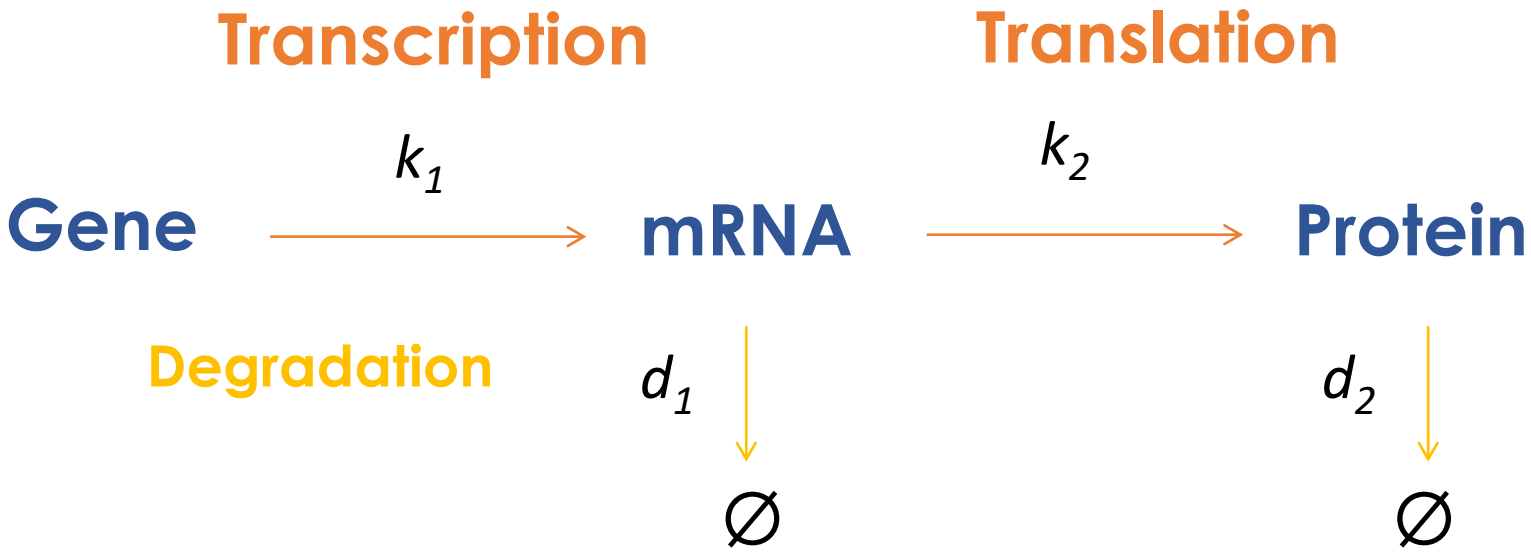
Translation of mRNA by Ribosomes

From Y. Boada (2018)

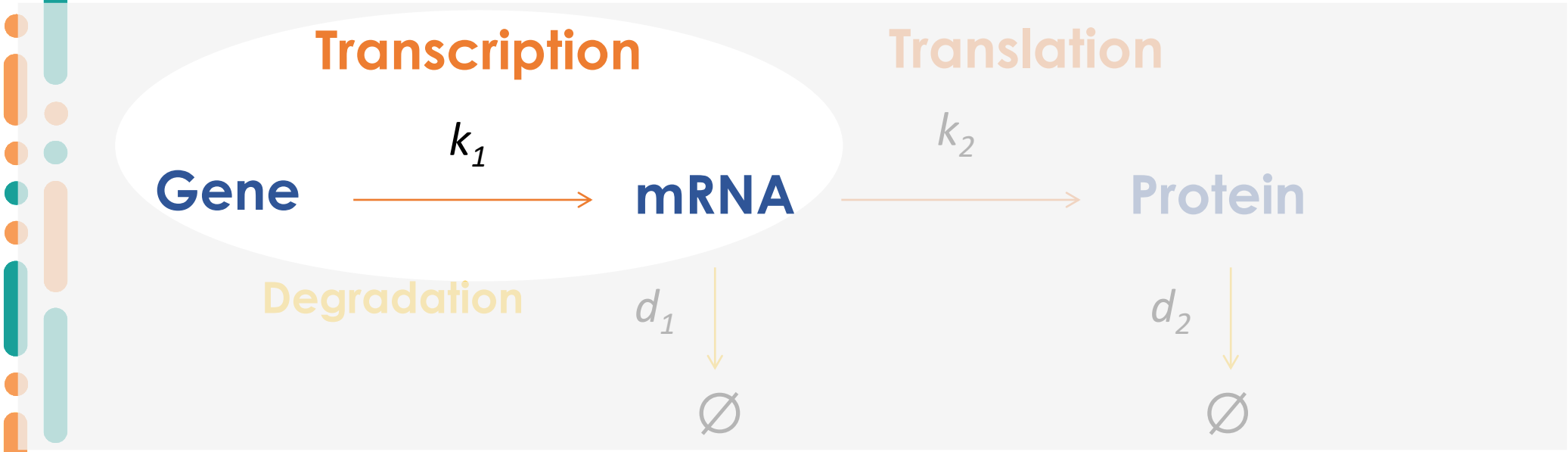
Constitutive gene expression (Simplified version)



Constitutive gene expression (Simplified version)

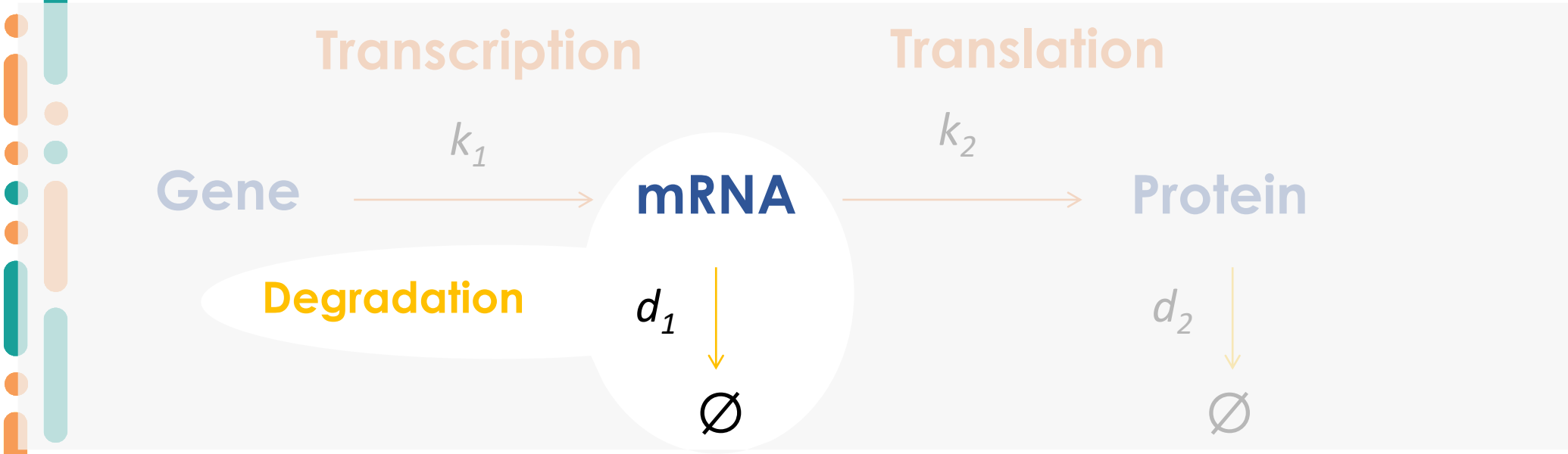


Constitutive gene expression (Simplified version)



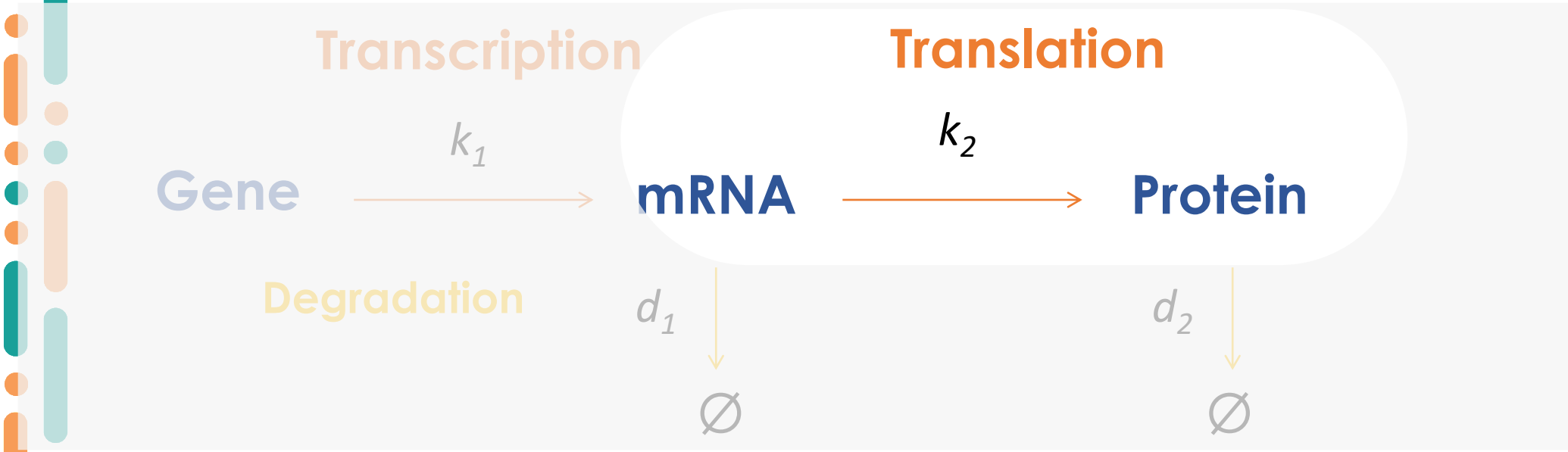
$$[\dot{\mathrm{mRNA}}] = k_1[\mathrm{Gene}]$$

Constitutive gene expression (Simplified version)



$$[\dot{\mathrm{mRNA}}] = k_1[\mathrm{Gene}] - d_1[\mathrm{mRNA}]$$

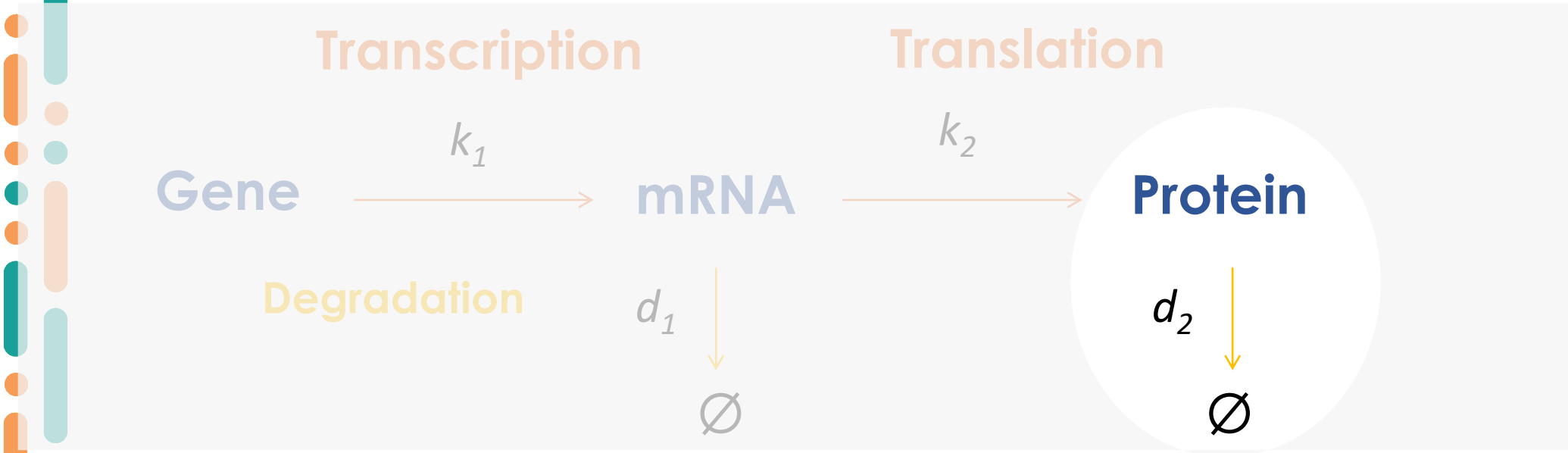
Constitutive gene expression (Simplified version)



$$\dot{[\text{mRNA}]} = k_1[\text{Gene}] - d_1[\text{mRNA}]$$

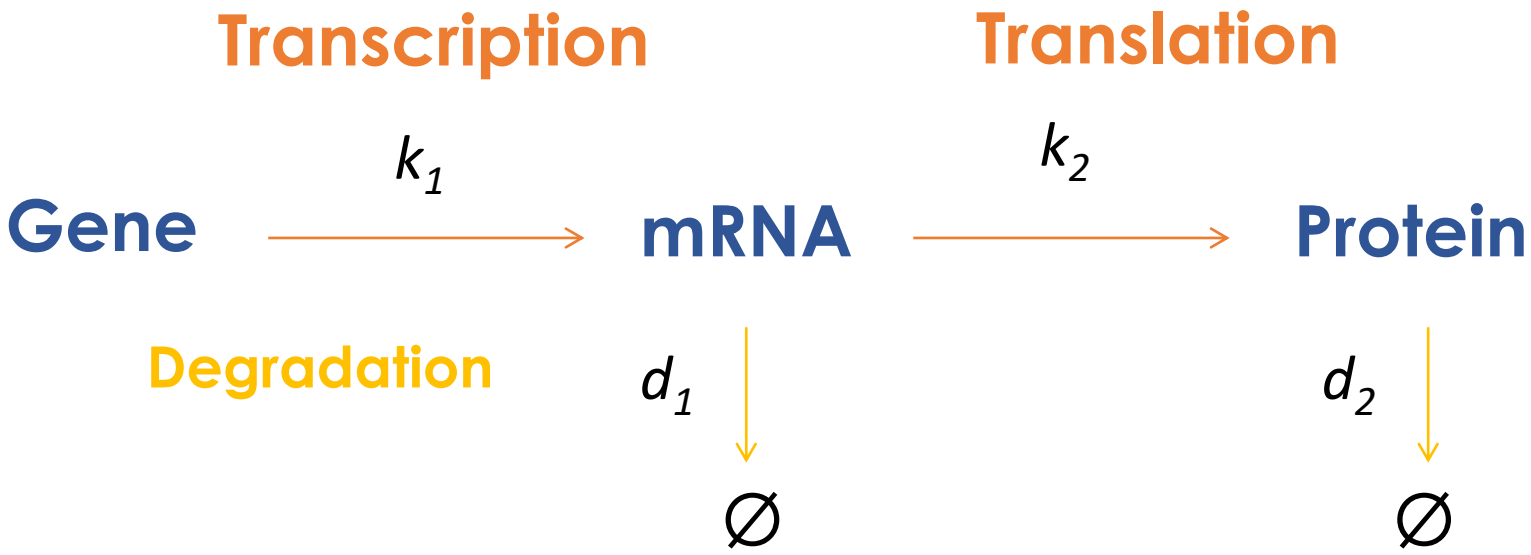
$$\dot{[\text{Protein}]} = k_2[\text{mRNA}]$$

Constitutive gene expression (Simplified version)



$$\dot{[\text{mRNA}]} = k_1[\text{Gene}] - d_1[\text{mRNA}]$$

$$\dot{[\text{Protein}]} = k_2[\text{mRNA}] - d_2[\text{Protein}]$$



$$\dot{[\text{mRNA}]} = k_1[\text{Gene}] - d_1[\text{mRNA}]$$

$$\dot{[\text{Protein}]} = k_2[\text{mRNA}] - d_2[\text{Protein}]$$

Constitutive gene expression - Remarks

$$\dot{[\text{mRNA}]} = k_1[\text{Gene}] - d_1[\text{mRNA}]$$

$$\dot{[\text{Protein}]} = k_2[\text{mRNA}] - d_2[\text{Protein}]$$

- [Gene] is considered a constant value and depends on: the Origin of Replication and the Plasmid Copy Number where the Gene is cloned.
- We are conidering:
  - RNA polymerase and Ribosomes are in sufficiently enough amount so that they are not limiting the kinetics.
  - Binding/Unbinding processes are much faster than transcription and translation.

Modeling I: ODEs and Hill Functions

Section 2: Derivation of the Hill Function

by Alejandro Vignoni (vignoni@isa.upv.es)

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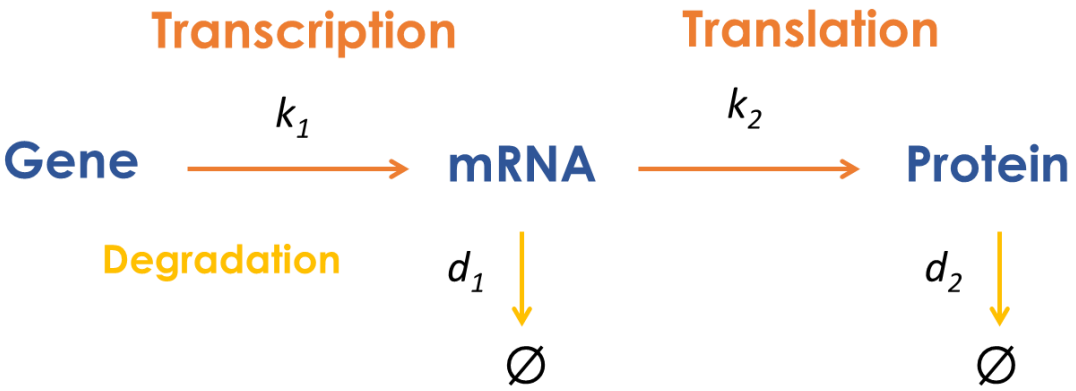
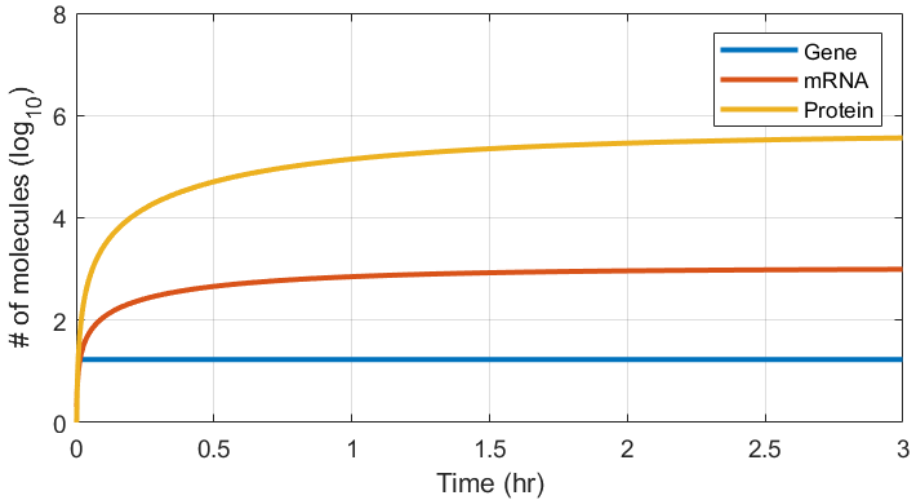
Today Webinar's Topics

- Section 1: ODEs, the law of mass action, and the central dogma (~15 min)
- Section 2: Derivation of a Hill function from the law of mass action (15 min)
- Section 3: Hill function examples and intuitions: effects of parameters on activators, repressors, hybrid promoters, using a Matlab exploration package. (15min)
- Q&A – (at the end of each 15 minutes block, total 15 min)

Remember: Constitutive gene expression

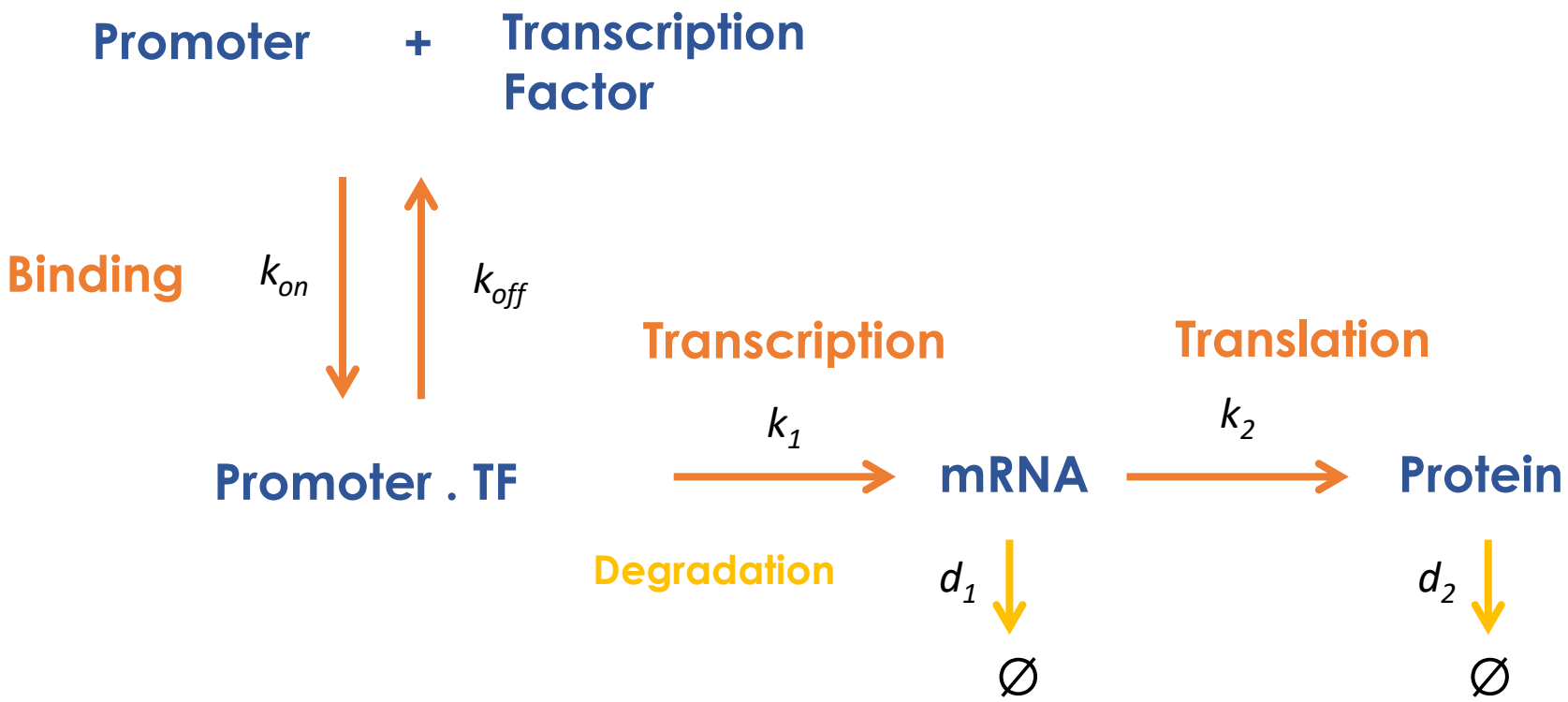




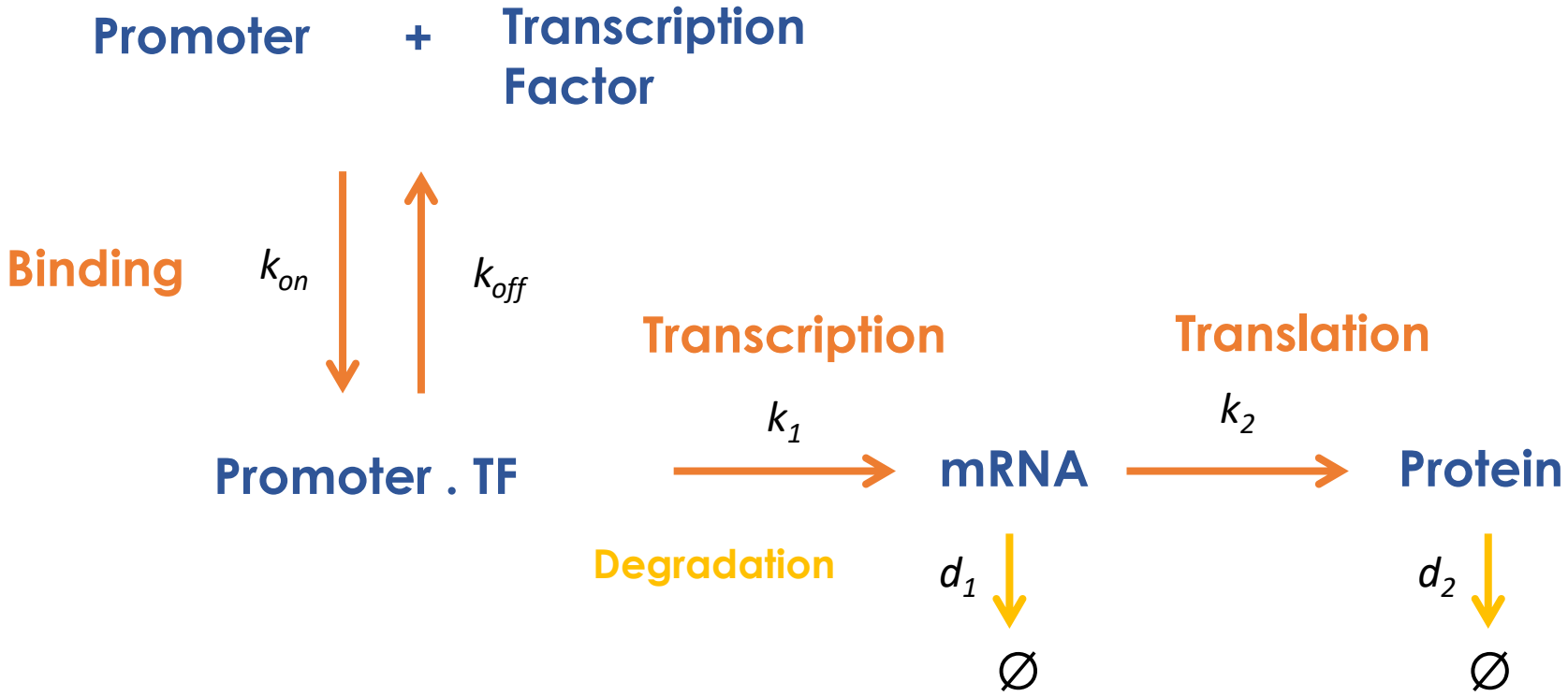
$$[\dot{\text{mRNA}}] = k_1[\text{Gene}] - d_1[\text{mRNA}]$$

$$[\dot{\text{Protein}}] = k_2[\text{mRNA}] - d_2[\text{Protein}]$$

Gene expression regulation by Transcription Factors (TF)



Gene expression regulation by Transcription Factors (TF)



We will get: -5 Equations
-with 7 parameters

Problems:

- k_1, k_2, d_1 and d_2 become indistinguishable when we measure only the protein amount.
- k_{on}, k_{off} are very difficult to measure.

Gene expression regulation by Transcription Factors (TF)

Promoter + **Transcription**

We want to approximate and simplify the problem and obtain a model easier to relate with experimental data:

1. We will obtain all the equations.
2. Approximate and reduce them.

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∅

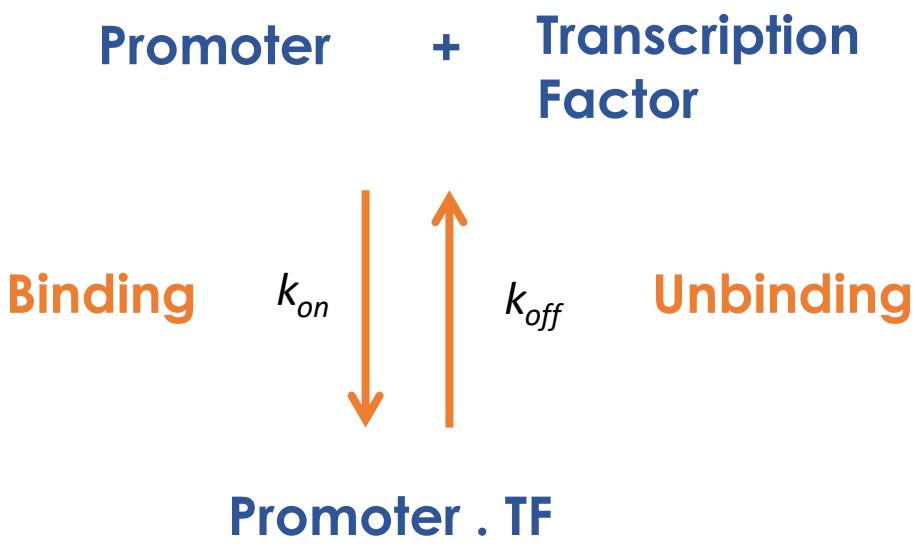
We will g

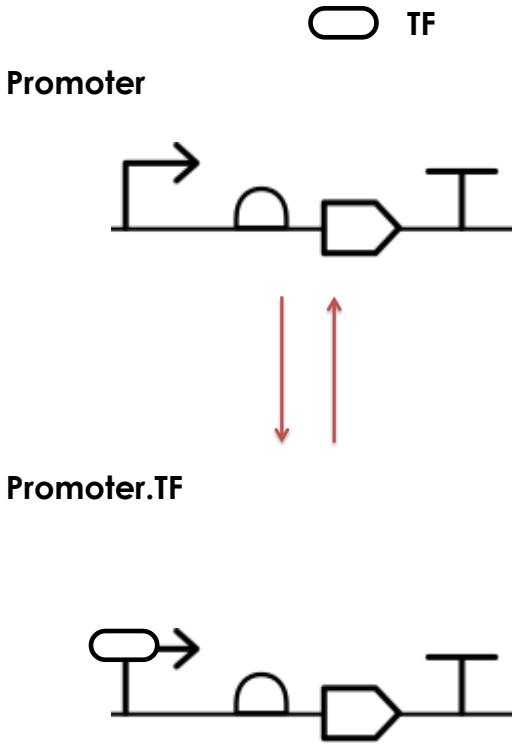
the protein amount.

Problems: → k_{on}, k_{off}, are very difficult to measure.

Gene expression regulation by Transcription Factors (TF)

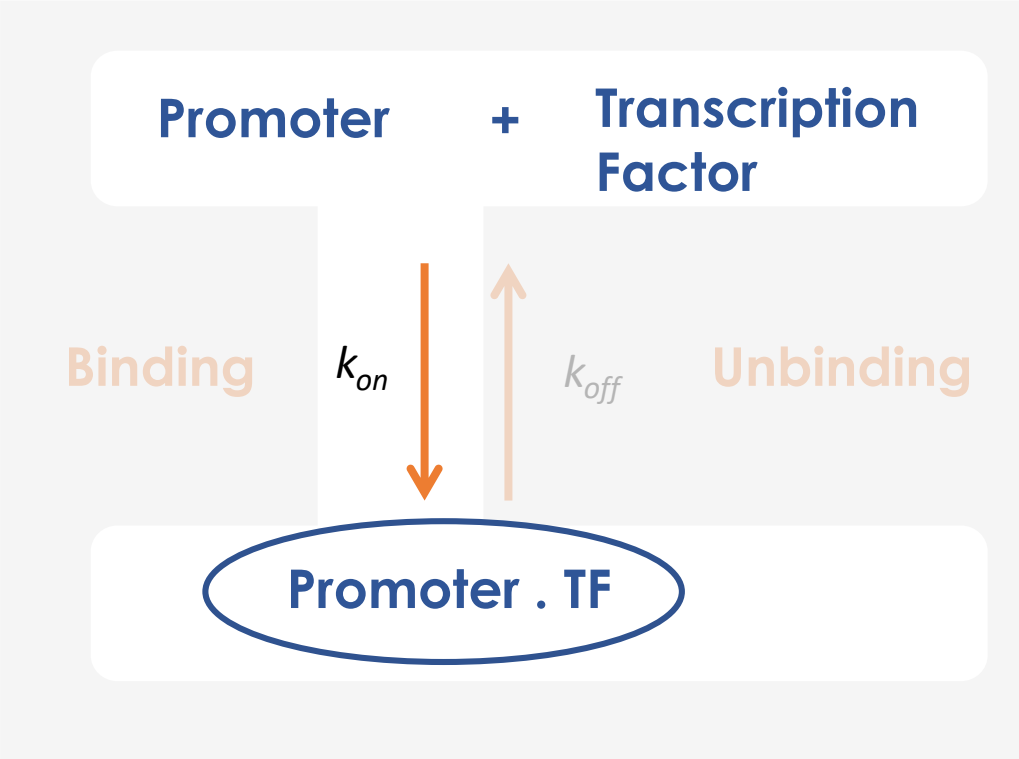
Part I: Getting the model





Gene expression regulation by Transcription Factors (TF)

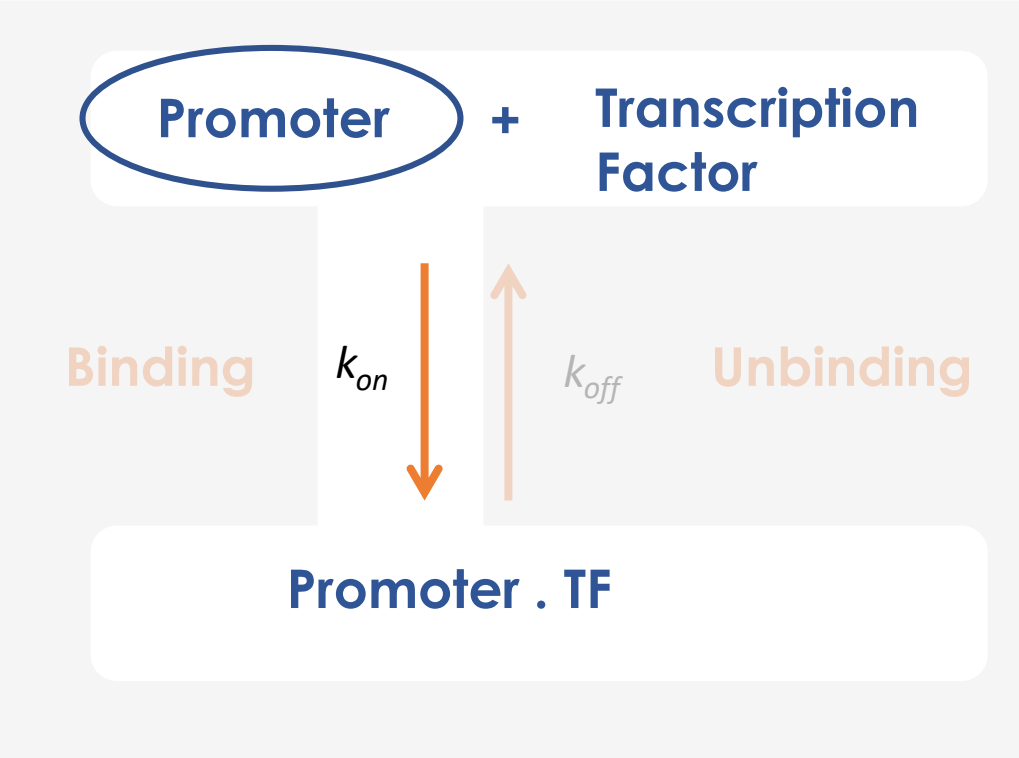
Part I: Getting the model



$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}]$$

Gene expression regulation by Transcription Factors (TF)

Part I: Getting the model

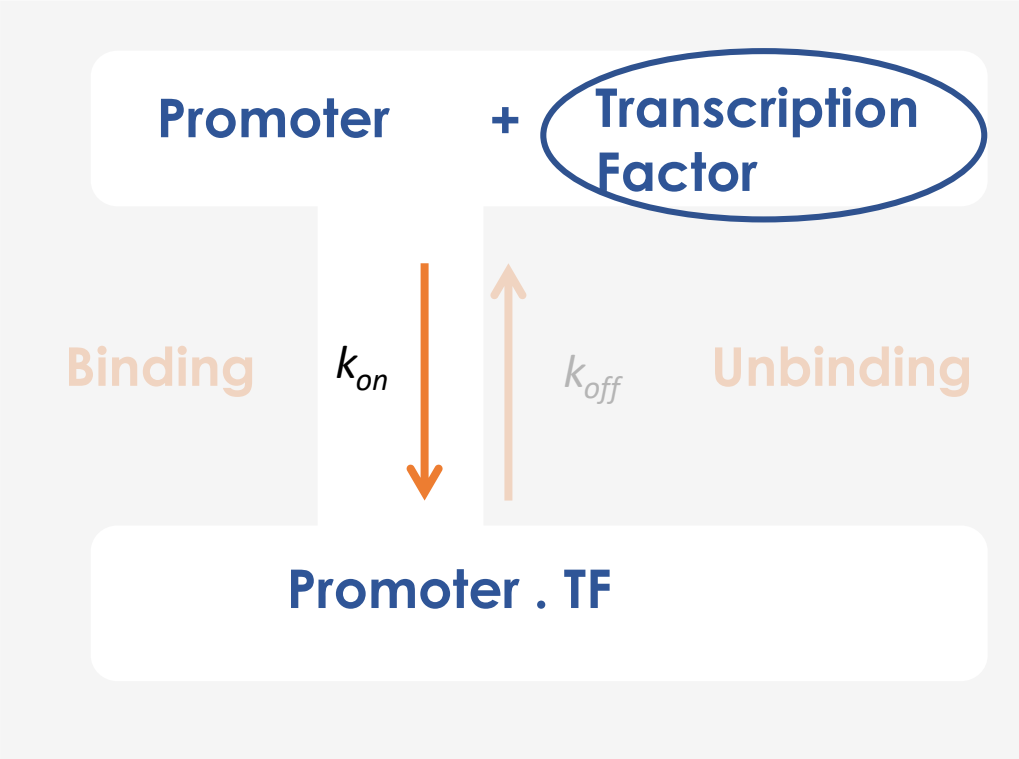


$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}]$$

$$[\dot{\text{Prom}}] = -k_{on}\,[\text{Prom}][\text{TF}]$$

Gene expression regulation by Transcription Factors (TF)

Part I: Getting the model



$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}]$$

$$[\dot{\text{Prom}}] = -k_{on}\,[\text{Prom}][\text{TF}]$$

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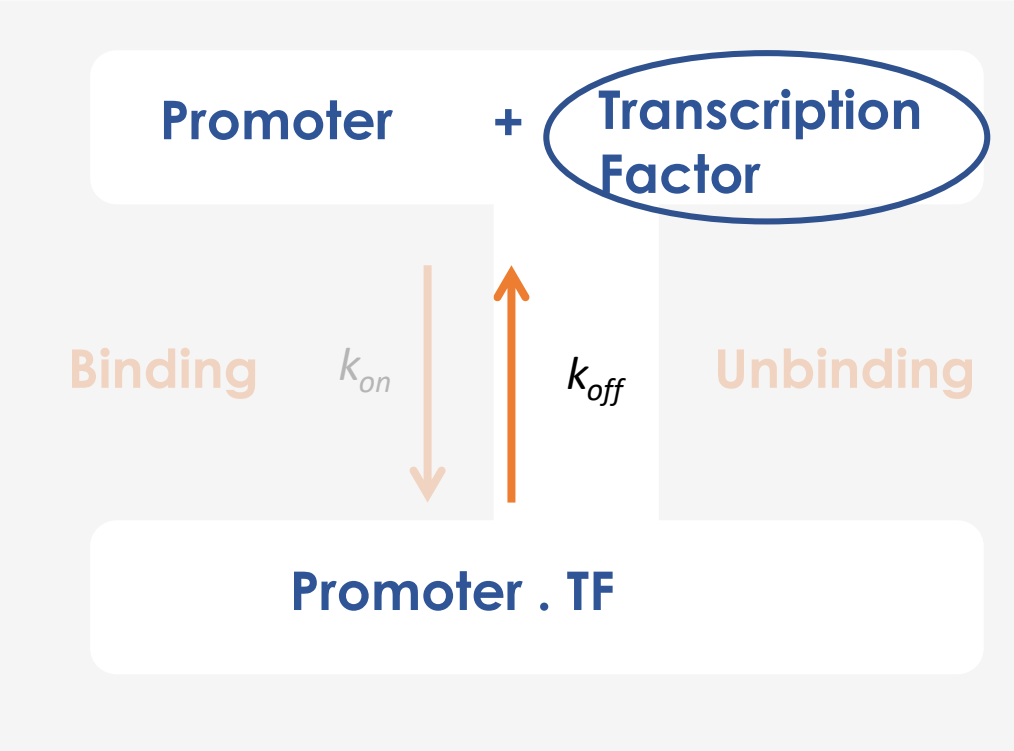
Gene expression regulation by Transcription Factors (TF)

Part I: Getting the model



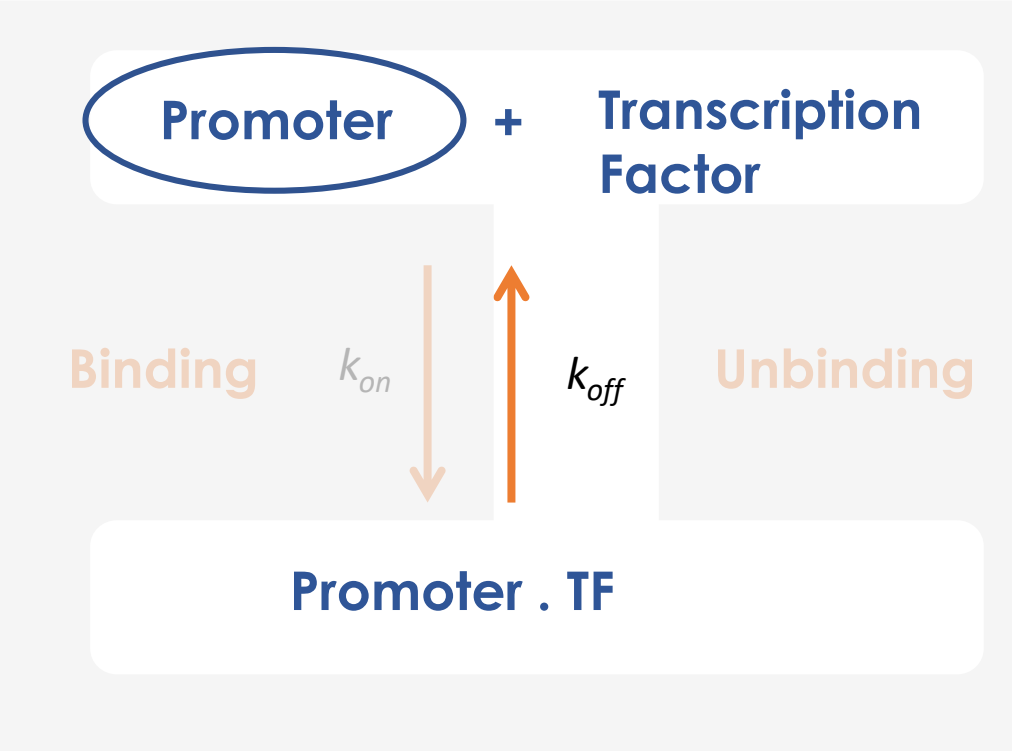
$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}]$$

$$[\dot{\text{Prom}}] = -k_{on}\,[\text{Prom}][\text{TF}]$$

$$[\dot{\text{TF}}] = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}\,[\text{Prom.TF}]$$

Gene expression regulation by Transcription Factors (TF)

Part I: Getting the model



$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}]$$

$$[\dot{\text{Prom}}] = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

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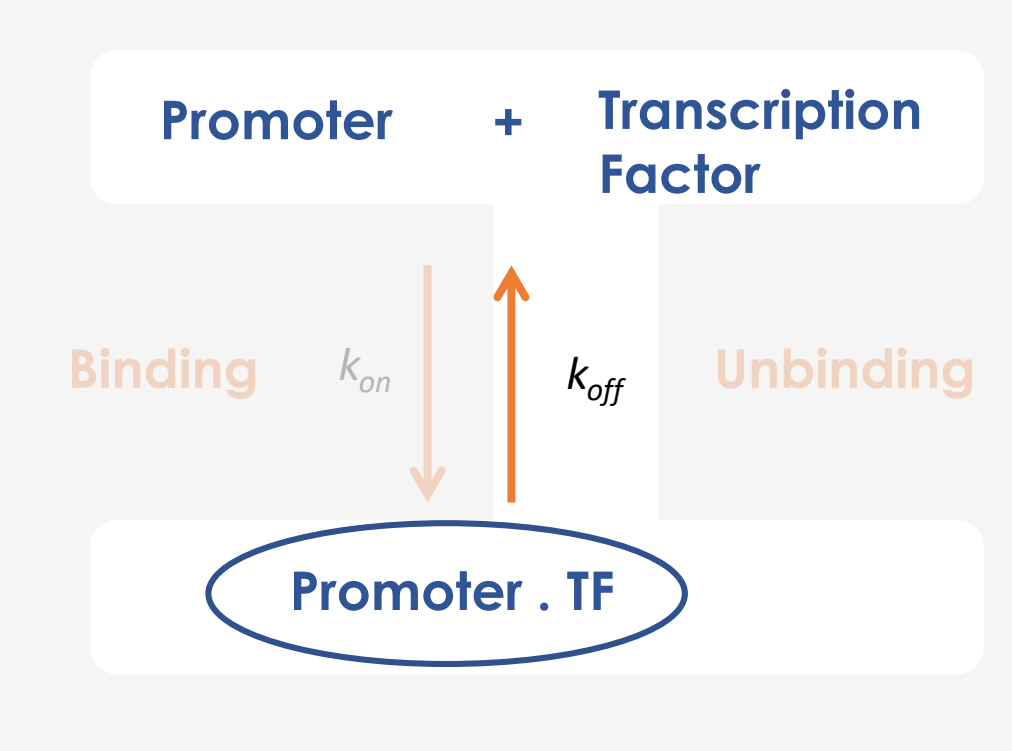
Gene expression regulation by Transcription Factors (TF)

Part I: Getting the model



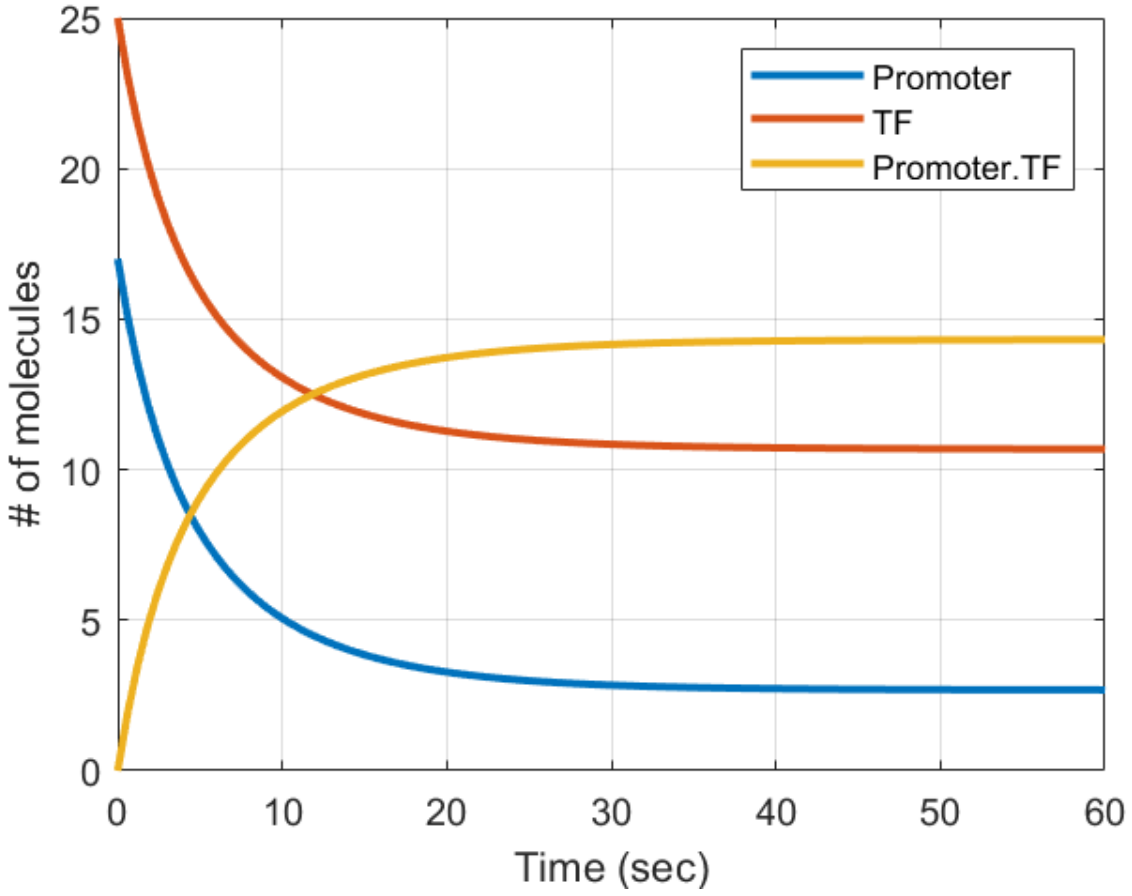
$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$

$$[\dot{\text{Prom}}] = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

$$[\dot{\text{TF}}] = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

Gene expression regulation by Transcription Factors (TF)

Part I: Simulation



$$[\dot{\text{Prom.TF}}] = k_{on}\,[\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$

$$[\dot{\text{Prom}}] = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

$$[\dot{\text{TF}}] = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

Starting with:
17 Promoters (Plasmid copy number)
25 molecules of Transcription Factor (TF)
k_{on} = 0.5 molecules^{-1} min^{-1}
k_{off} = 1 min^{-1}

`Main_TF.m`

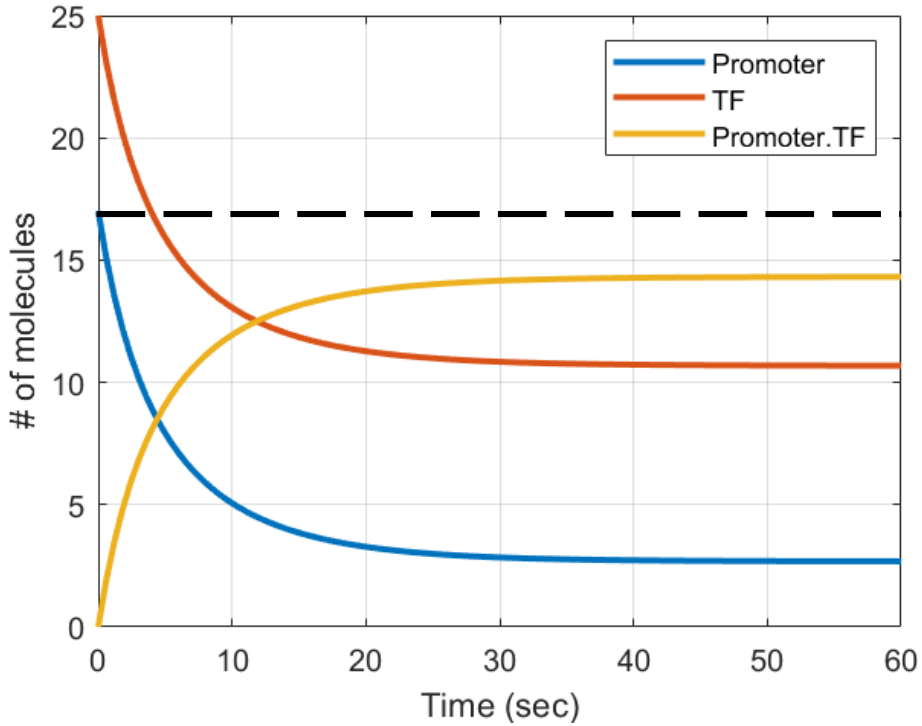
Gene expression regulation by Transcription Factors (TF)

Part II: Model reduction

$$\dot{[\text{Prom}]} = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

$$\dot{[\text{TF}]} = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

$$\dot{[\text{Prom.TF}]} = \quad k_{on}\,[\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$



Remarks

- First two equations are equal (Blue and red)!
- The sum of the first one and the third one is identically zero (Blue and yellow)!
- We can use this fact (promoter invariance) to simplify the equations and reduce the model.

Gene expression regulation by Transcription Factors (TF)

Part II: Model reduction

Promoter invariance (constant Plasmid Copy Number)

$$\dot{[\text{Prom}]} = -k_{on}\,[\text{Prom}][\text{TF}] + k_{off}[\text{Prom.TF}]$$

$$+$$

$$\dot{[\text{Prom.TF}]} = \quad k_{on}\,[\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$

$$\dot{[\text{Prom.TF}]} + \dot{[\text{Prom}]} = 0$$

Integrating this…

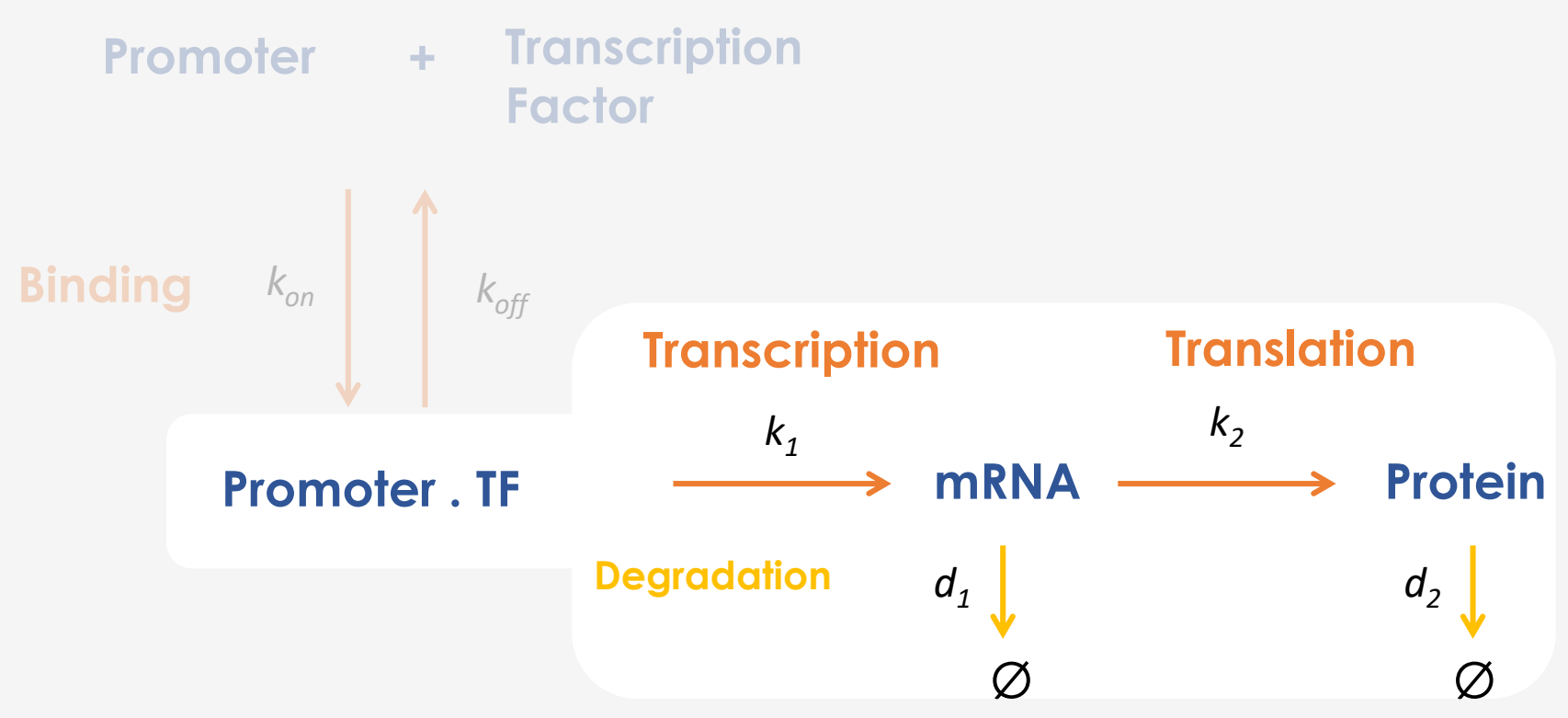
$$[\text{Prom.TF}] + [\text{Prom}] = C_N$$ ← Plasmid Copy Number

$$[\text{Prom}] = C_N - [\text{Prom.TF}]$$

Save this one, we will use it later.

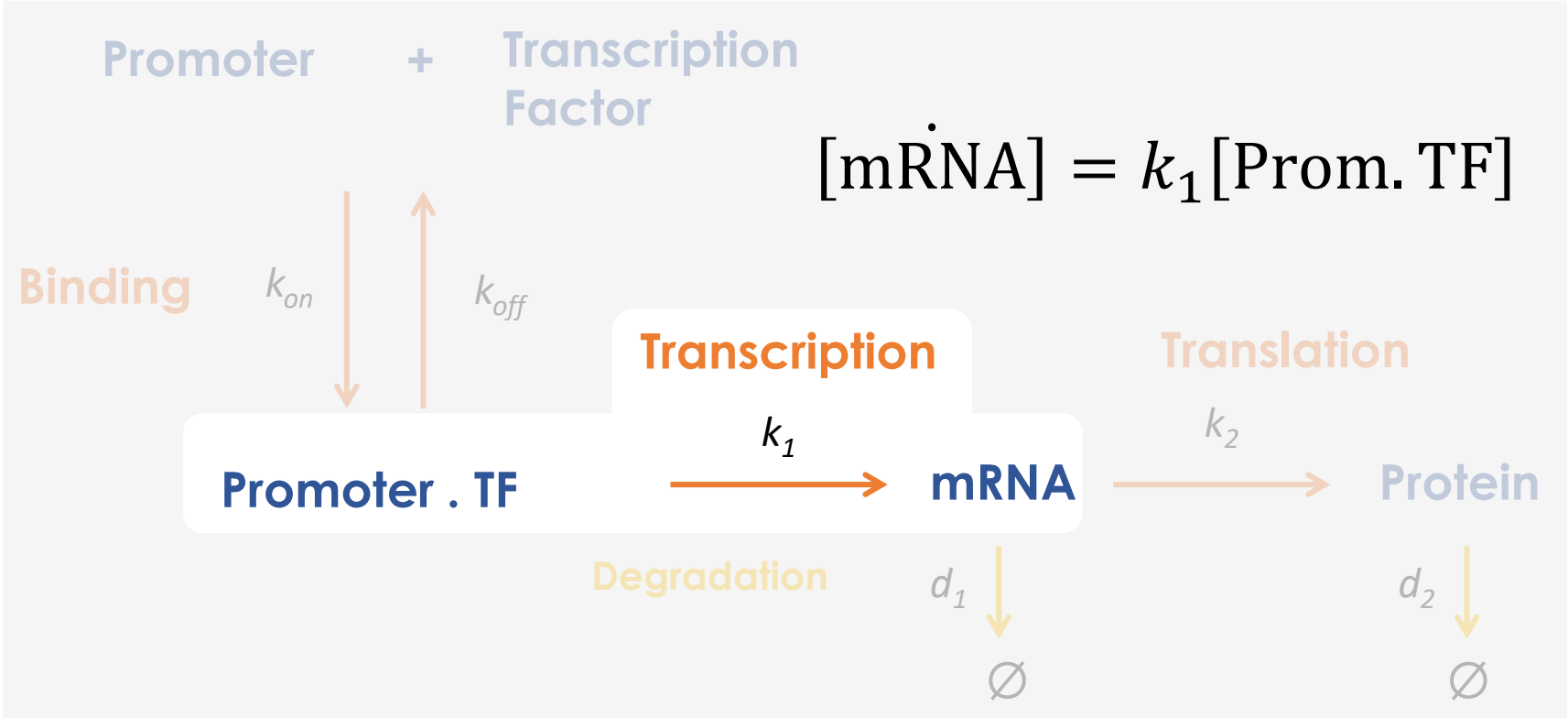
Gene expression regulation by Transcription Factors (TF)

Part I: Getting the Model



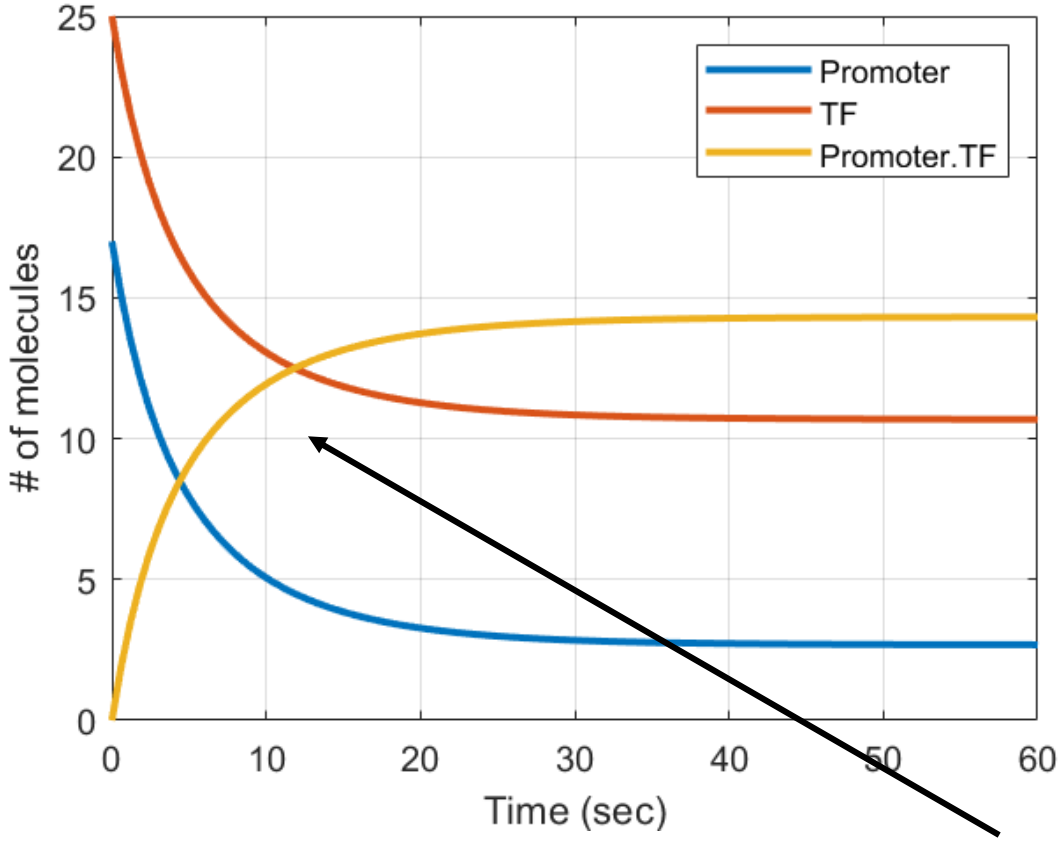
Gene expression regulation by Transcription Factors (TF)

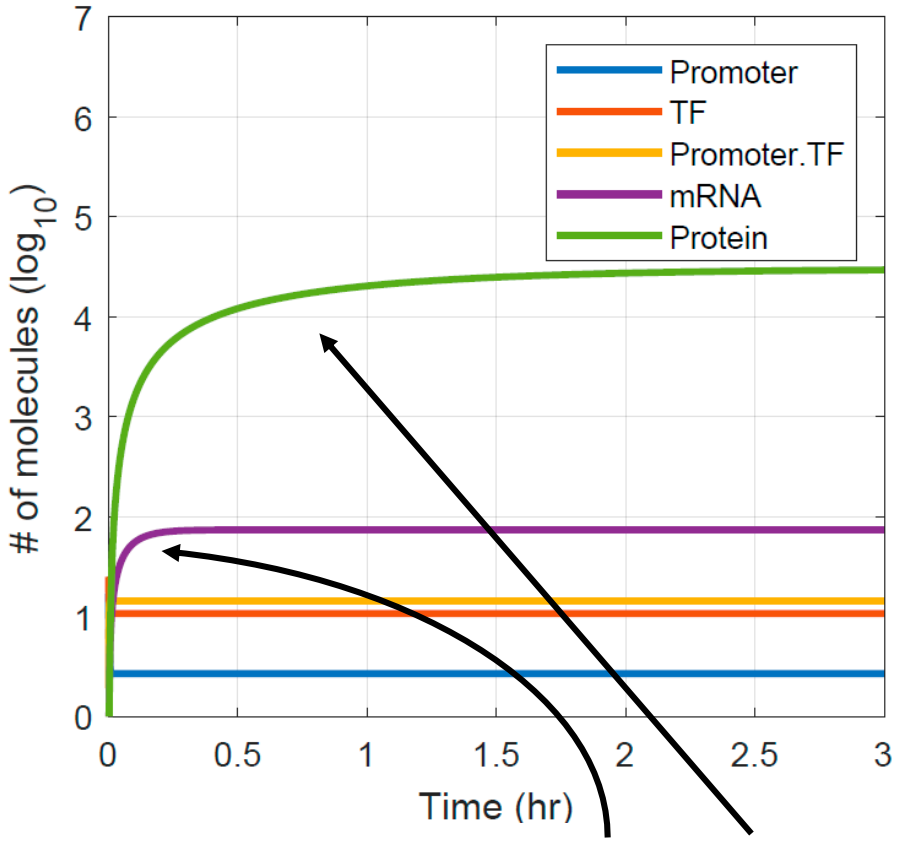
Part I: Getting the Model



Gene expression regulation by Transcription Factors (TF)

Part I: Simulation





Note the difference in time scales: Binding in the seconds, transcription/translation from minutes to hours.

Gene expression regulation by Transcription Factors (TF)

Part II: Model reduction

Fast Transcription Factor – Promoter binding

$$[\dot{\text{Prom.TF}}] \approx 0$$

Because of the difference in time scales: Binding in the seconds, transcription/translation from minutes to hours; we can say that TF rapidly binds to the promoter and this reaction reaches equilibrium very fast.
This is called Quasy Steady State Approximation (QSSA).

$$[\dot{\text{Prom.TF}}] = k_{on}\ [\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$

$$0 = k_{on}\ [\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$

From invariance (previous slide)

$$[\text{Prom}] = C_N - [\text{Prom.TF}]$$

Using these two, we will derive the Hill function

Gene expression regulation by Transcription Factors (TF)

Part II: Model reduction

Replacing the free promoter equation into the TF bound Promoter one:

$$[\text{Prom}] = C_N - [\text{Prom.TF}]$$

$$0 = k_{on}\ [\text{Prom}][\text{TF}] - k_{off}[\text{Prom.TF}]$$

$$0 = k_{on}\ (C_N - [\text{Prom.TF}])[\text{TF}] - k_{off}[\text{Prom.TF}]$$

Gene expression regulation by Transcription Factors (TF)

Part II: Model reduction

Solving for the TF bound Promoter:

$$k_{on}\,(C_N - [\text{Prom. TF}])[\text{TF}] = k_{off}[\text{Prom. TF}]$$

$$k_{on}\,[\text{TF}]C_N - k_{on}\,[\text{TF}][\text{Prom. TF}] = k_{off}[\text{Prom. TF}]$$

$$k_{on}\,[\text{TF}]C_N = k_{on}\,[\text{TF}][\text{Prom. TF}] + k_{off}[\text{Prom. TF}]$$

A bit of algebra...

$$k_{on}\,[\text{TF}]C_N = \left(k_{on}\,[\text{TF}] + k_{off}\right)[\text{Prom. TF}]$$

$$[\text{Prom. TF}] = C_N \frac{k_{on}[\text{TF}]}{k_{on}\,[\text{TF}]+k_{off}} = C_N \frac{[\text{TF}]}{\frac{k_{off}}{k_{on}}+[\text{TF}]} = C_N \frac{[\text{TF}]}{K_d+[\text{TF}]}$$

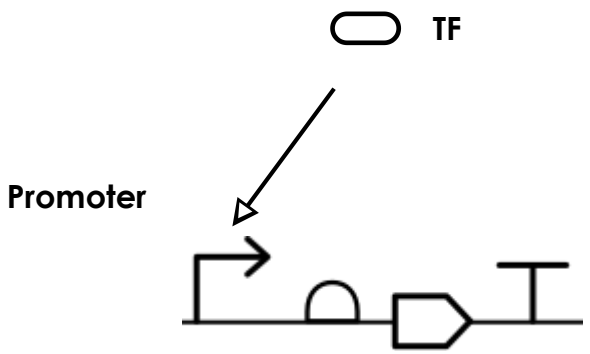
Gene expression regulation by Transcription Factors (TF)

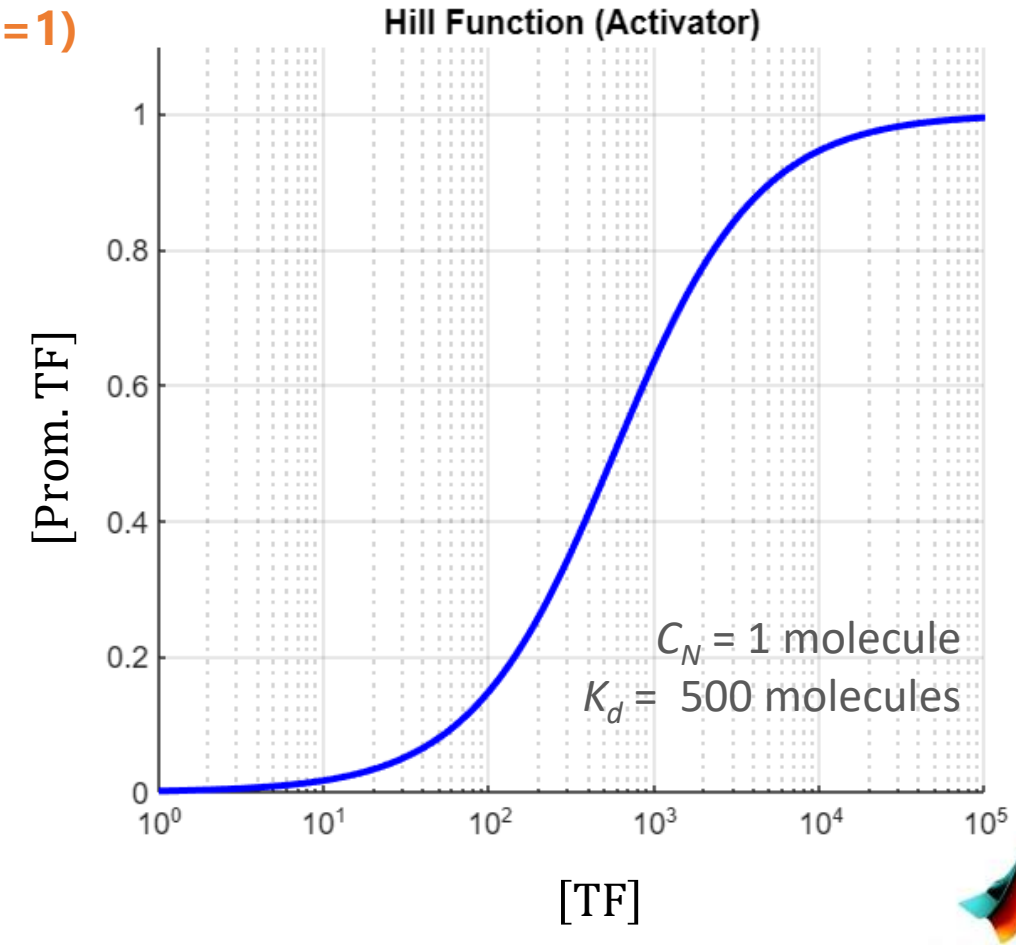
Part II: Model reduction

We get the Hill function (with Hill coefficient n=1)

$$[\text{Prom. TF}] = C_N \frac{[\text{TF}]}{K_d + [\text{TF}]}$$

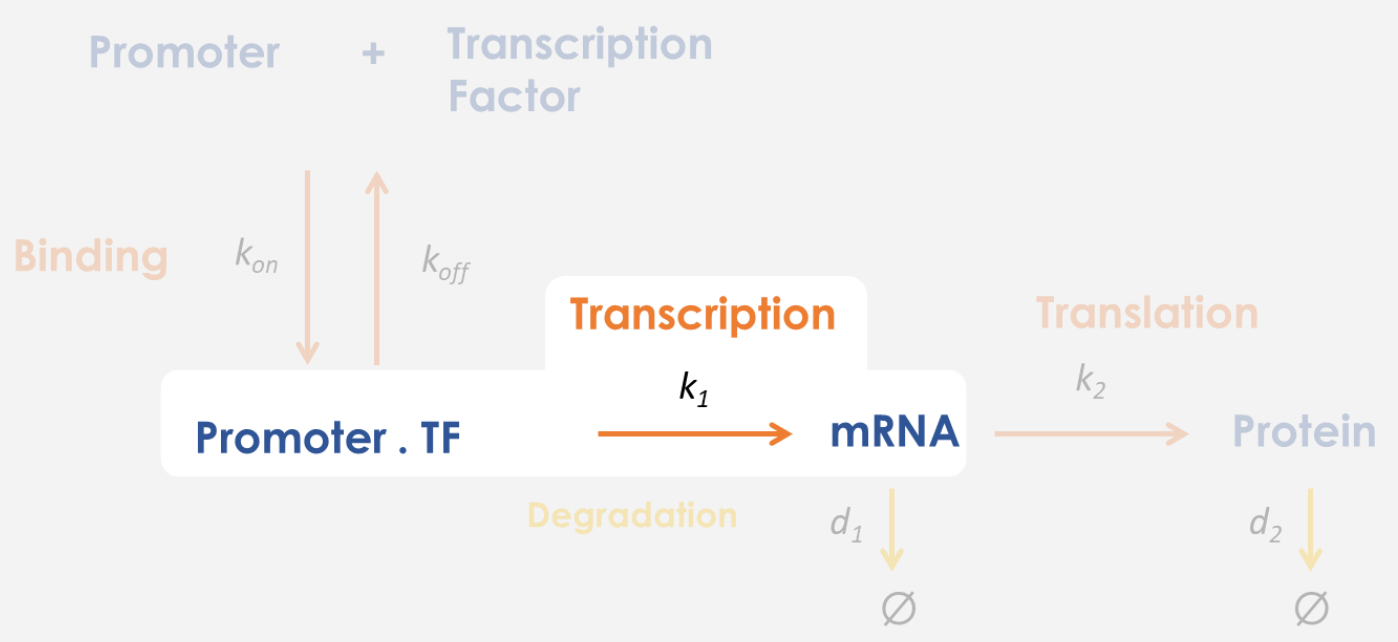
Activator





Gene expression regulation by Transcription Factors (TF)

Part II: Model reduction



$$[\dot{\mathrm{mRNA}}] = k_1[\mathrm{Prom.TF}]$$

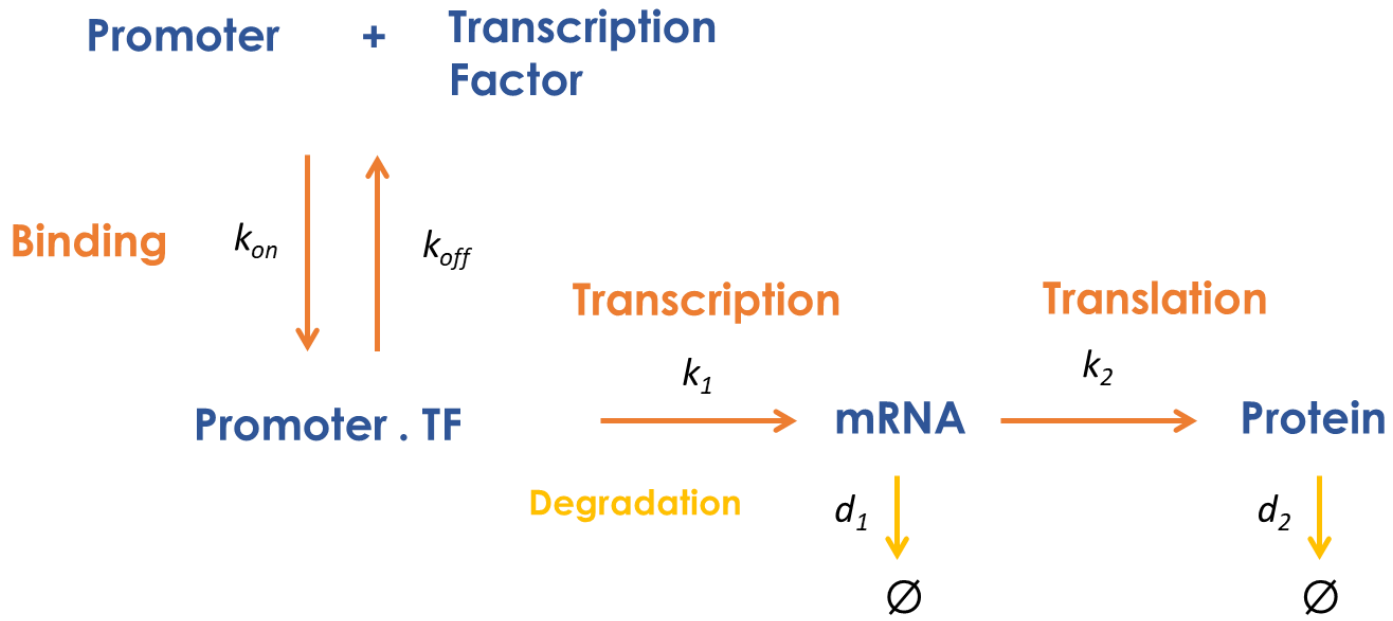
$$[\mathrm{Prom.TF}] = C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]}$$

The complete equation for the mRNA

$$[\dot{\mathrm{mRNA}}] = k_1 \, C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]} - d_1[\mathrm{mRNA}]$$

Gene expression regulation by Transcription Factors (TF)

Part I: Getting the Model

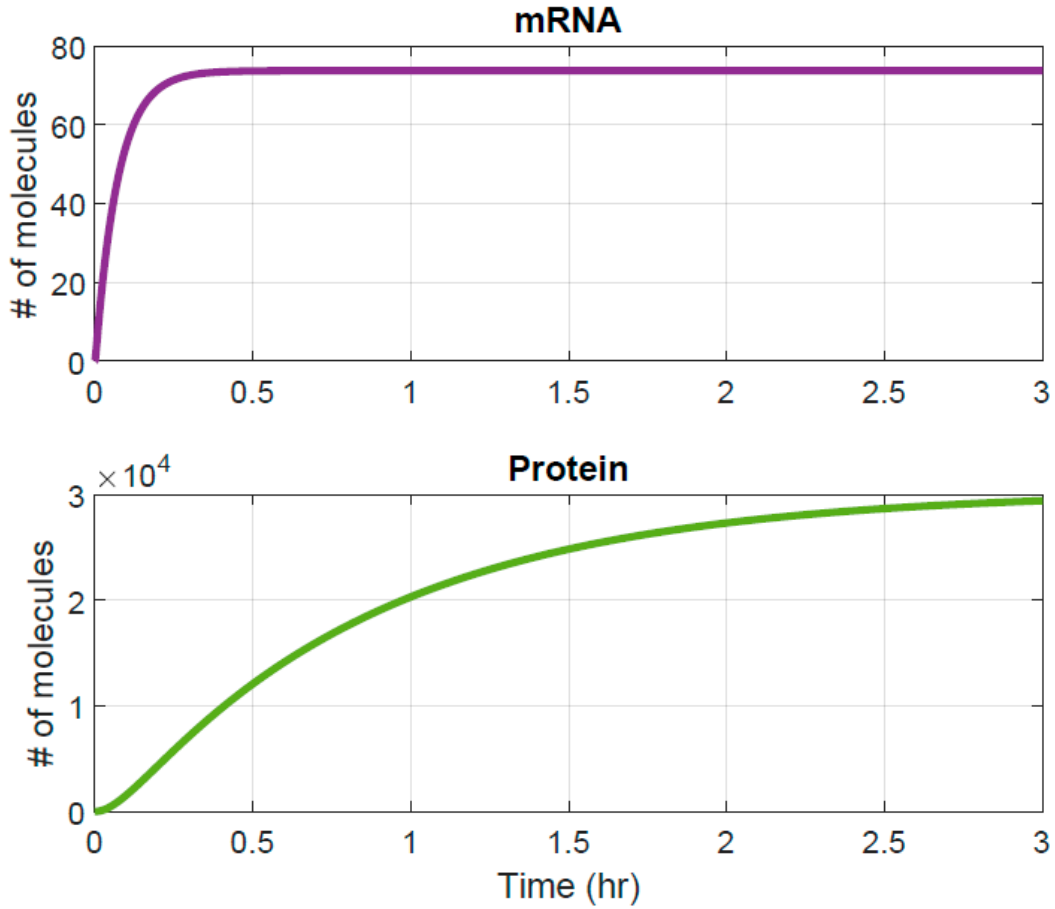


$$\frac{d[\mathrm{mRNA}]}{dt} = [\dot{\mathrm{mRNA}}] = k_1 \, C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]} - d_1[\mathrm{mRNA}]$$

$$\frac{d[\mathrm{Protein}]}{dt} = [\dot{\mathrm{Protein}}] = k_2[\mathrm{mRNA}] - d_2[\mathrm{Protein}]$$

Gene expression regulation by Transcription Factors (TF)

Part I: Simulation



$$[\dot{\mathrm{mRNA}}] = k_1 \, C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]} - d_1[\mathrm{mRNA}]$$

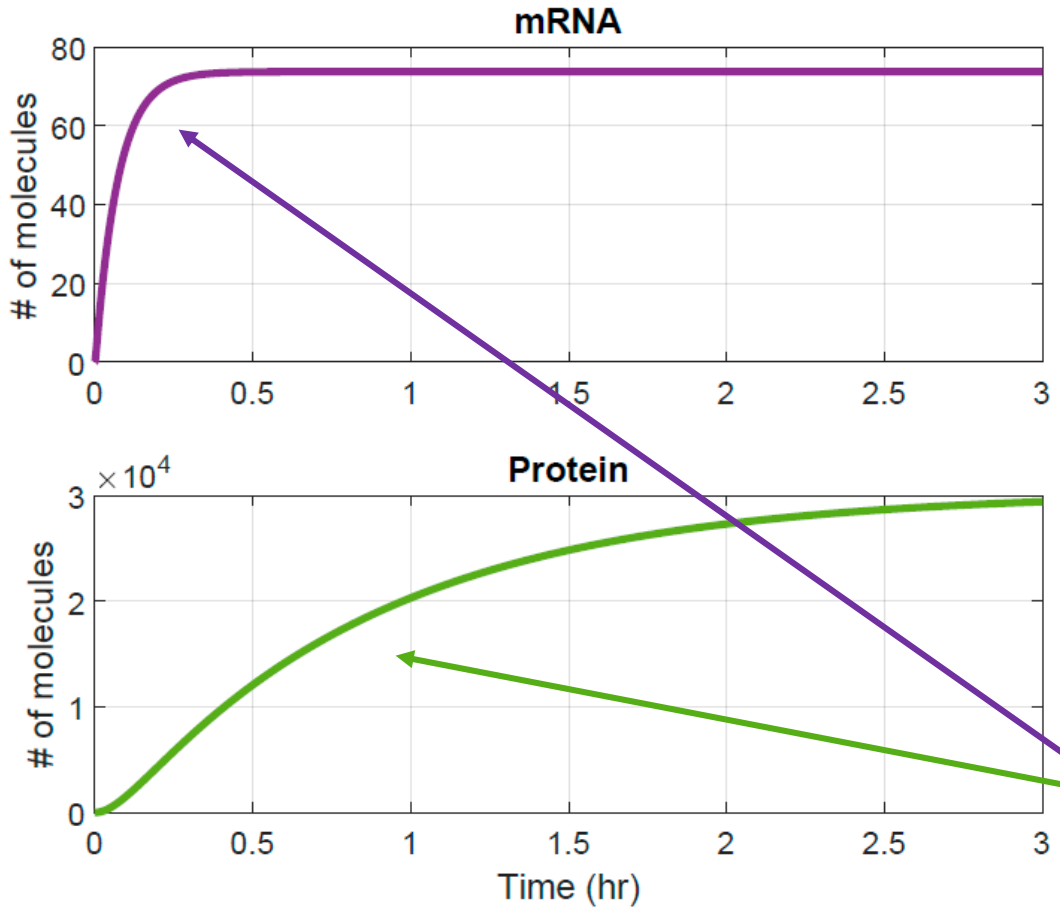
$$[\dot{\mathrm{Protein}}] = k_2[\mathrm{mRNA}] - d_2[\mathrm{Protein}]$$

Parameters:
CN = 17 molecules (Plasmid copy number)
Kd = 2 molecules
TF = 25 molecules (Transcription Factor)
The other parameters same than constitutive

`Main_TF.m`

Gene expression regulation by Transcription Factors (TF)

Part I: Simulation



$$[\dot{\mathrm{mRNA}}] = k_1 \, C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]} - d_1[\mathrm{mRNA}]$$

$$[\dot{\mathrm{Protein}}] = k_2[\mathrm{mRNA}] - d_2[\mathrm{Protein}]$$

Parameters:
CN = 17 molecules (Plasmid copy number)
Kd = 2 molecules
TF = 25 molecules (Transcription Factor)
The other parameters same than constitutive

Note the difference in time scales: transcription (mRNA) in minutes, translation (Protein) hours.

`Main_TF.m`

Gene expression regulation by Transcription Factors (TF)

Now, as mRNA is much faster than Protein production… we use the same trick than before (QSSA):

$$[\dot{\mathrm{mRNA}}] \approx 0$$

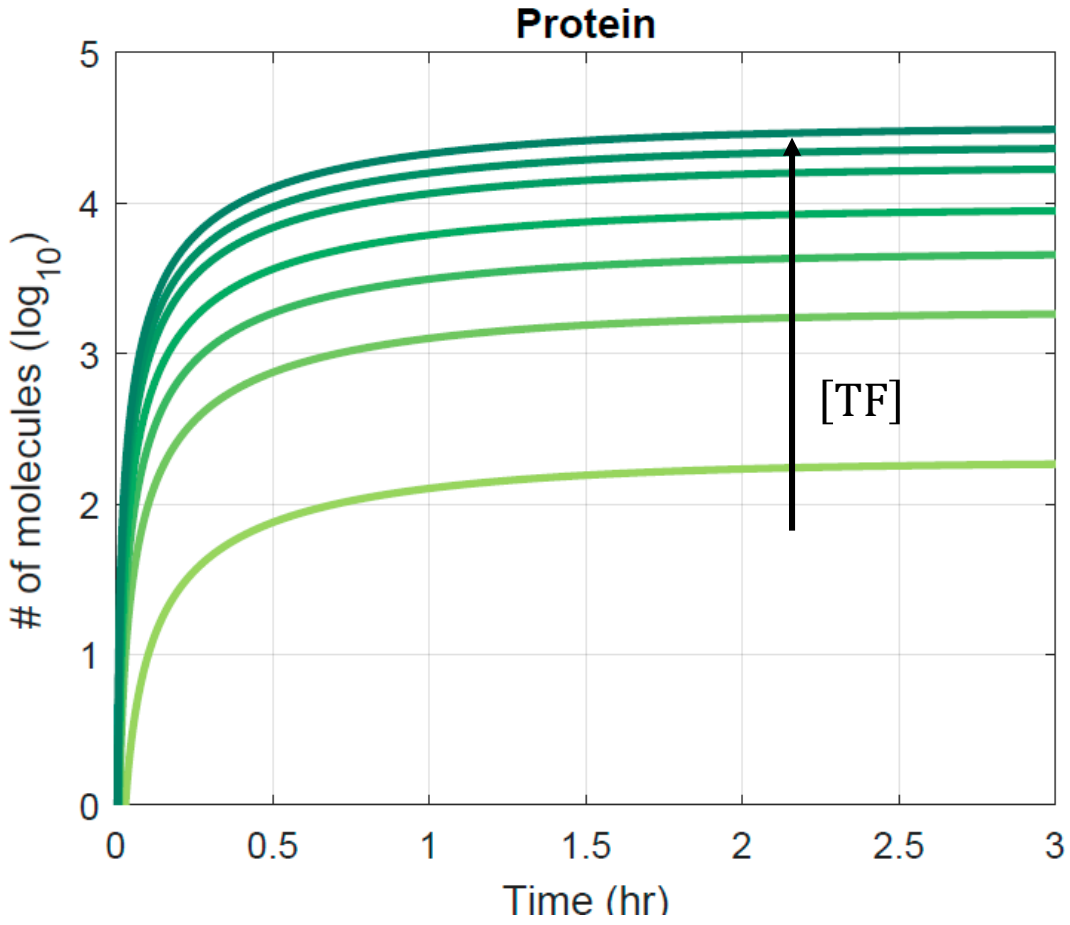
$$0 = k_1\ C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]} - d_1[\mathrm{mRNA}] \Rightarrow [\mathrm{mRNA}] = \frac{k_1}{d_1}\ C_N \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]}$$

$$\frac{d[\mathrm{Protein}]}{dt} = [\dot{\mathrm{Protein}}] = \alpha\ \frac{[\mathrm{TF}]}{K_d + [\mathrm{TF}]} - d_2[\mathrm{Protein}]$$

$$\alpha = k_2 \frac{k_1}{d_1} C_N$$

Gene expression regulation by Transcription Factors (TF)

Simulation



$$\dot{[\text{Protein}]} = \alpha \frac{[\text{TF}]}{K_d + [\text{TF}]} - d_2[\text{Protein}]$$

$$\alpha = k_2 \frac{k_1}{d_1} C_N$$

With:

α = 720 molecules min^{-1}

K_d = 2 molecules

d_2 = 0.02 min^{-1}

(this means 34 min of doubling time)

[TF]: from 0.1 molecule to 25 molecules of Transcription Factor

`Main_TF_vector.m`

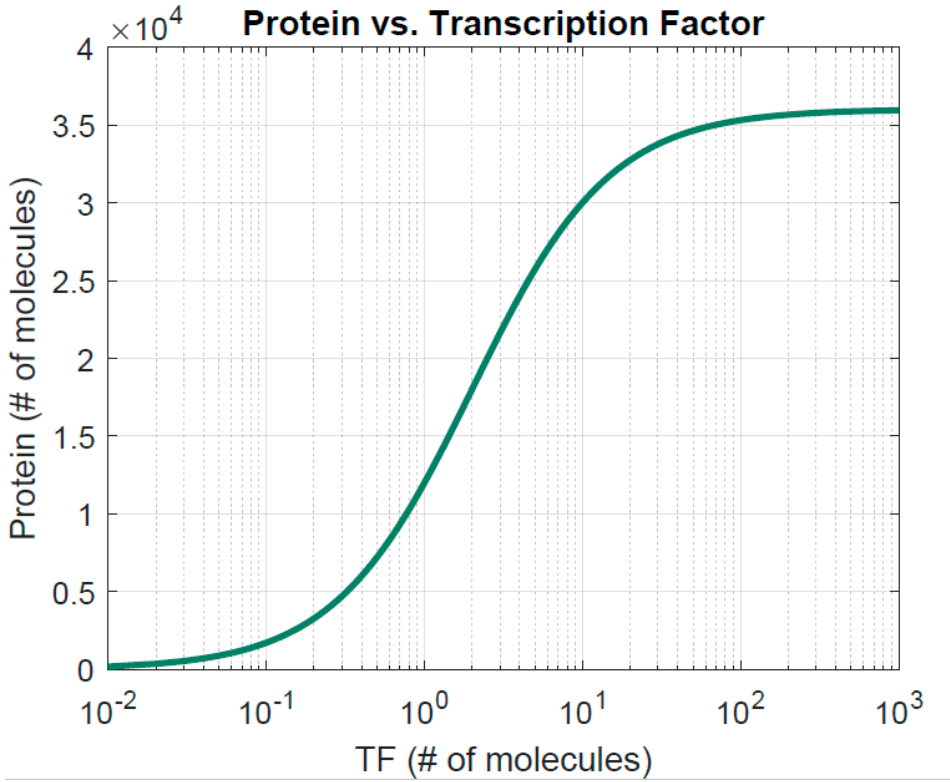
Gene expression regulation by Transcription Factors (TF)

Now, if we want the steady state we can use the same trick (QSSA) that we used before (equilibrium expression of protein, data at the end of the experiment)

$$\dot{[\text{Protein}]} \approx 0$$

$$[\text{Protein}] = \frac{\alpha}{d_2} \frac{[\text{TF}]}{K_d + [\text{TF}]}$$

$$\alpha = k_2 \frac{k_1}{d_1} C_N$$



protein_vs_TF.m

Modeling I: ODEs and Hill Functions

Section 3: Hill function examples and intuitions

by Alejandro Vignoni (vignoni@isa.upv.es)

An iGEM Engineering Committee Webinar

Webinar 2, May 25th, 2021

sb2cl Lab

Synthetic Biology and Biosystems Control Lab
Valencia UPV

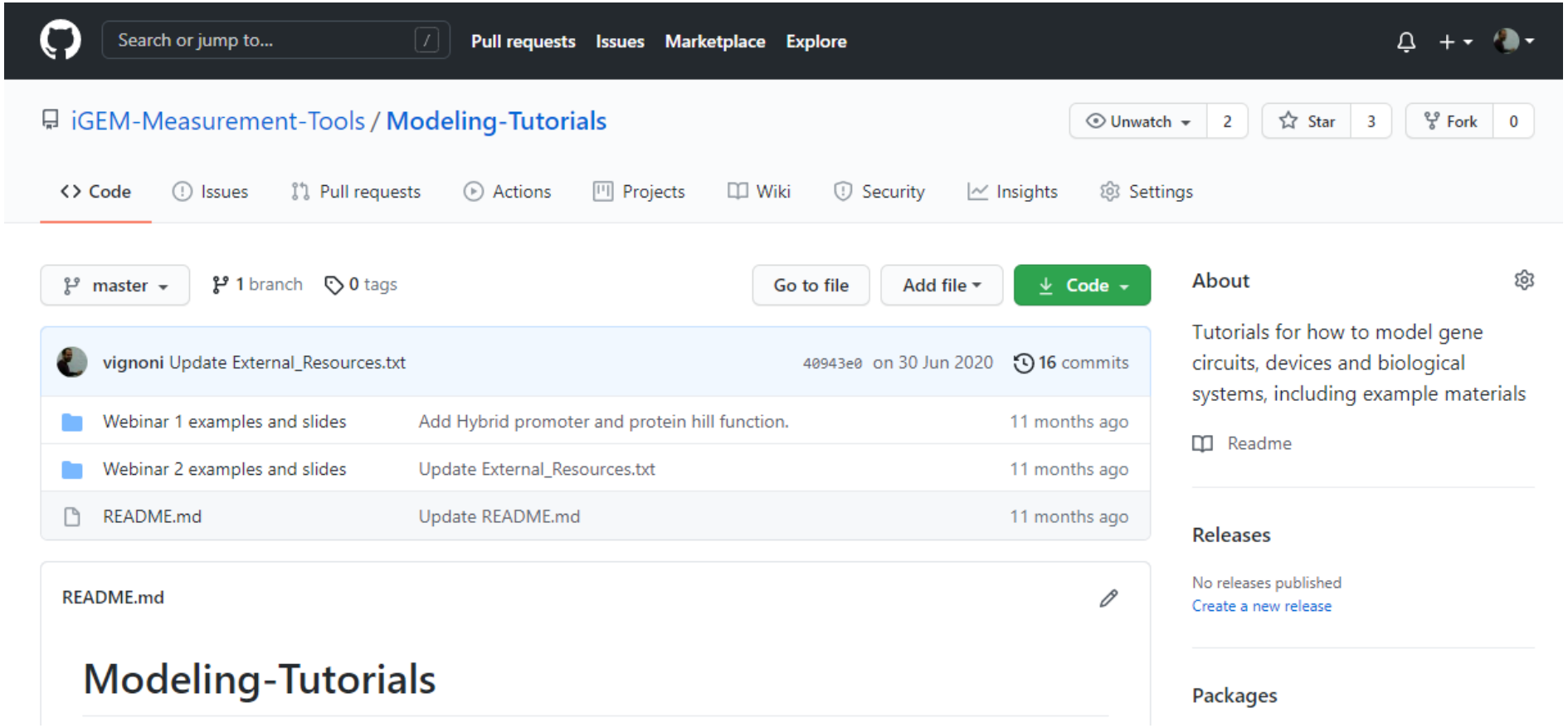
ai2 INSTITUTO DE AUTOMÁTICA E INFORMÁTICA INDUSTRIAL

UNIVERSIDAD POLITECNICA DE VALENCIA

Today Webinar's Topics

- Section 1: ODEs, the law of mass action, and the central dogma (~15 min)
- Section 2: Derivation of a Hill function from the law of mass action (15 min)
- Section 3: Hill function examples and intuitions: effects of parameters on activators, repressors, hybrid promoters, using a Matlab exploration package. (15min)
- Q&A – (at the end of each 15 minutes block, total 15 min)

Matlab exploration packages and resources:



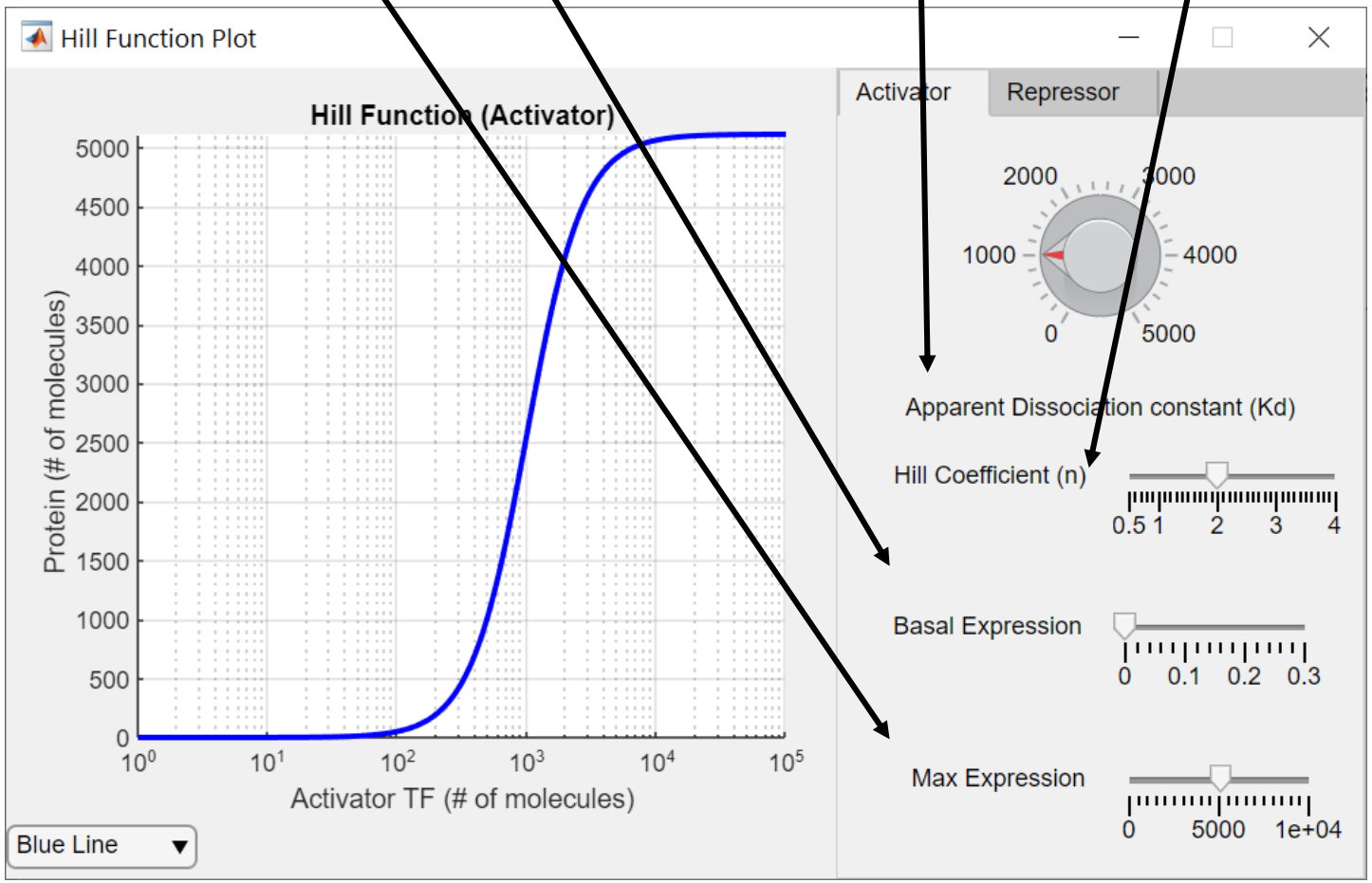
https://github.com/iGEM-Measurement-Tools/Modeling-Tutorials

Gene expression regulation by Transcription Factors (TF)

Activator

$$[\text{Protein}] = \alpha_{max}\left(\beta_0 + (1-\beta_0)\frac{[\text{TF}]^n}{K_d + [\text{TF}]^n}\right)$$

$$\alpha_{max} = k_2 \frac{k_1}{d_1 d_2} C_N$$



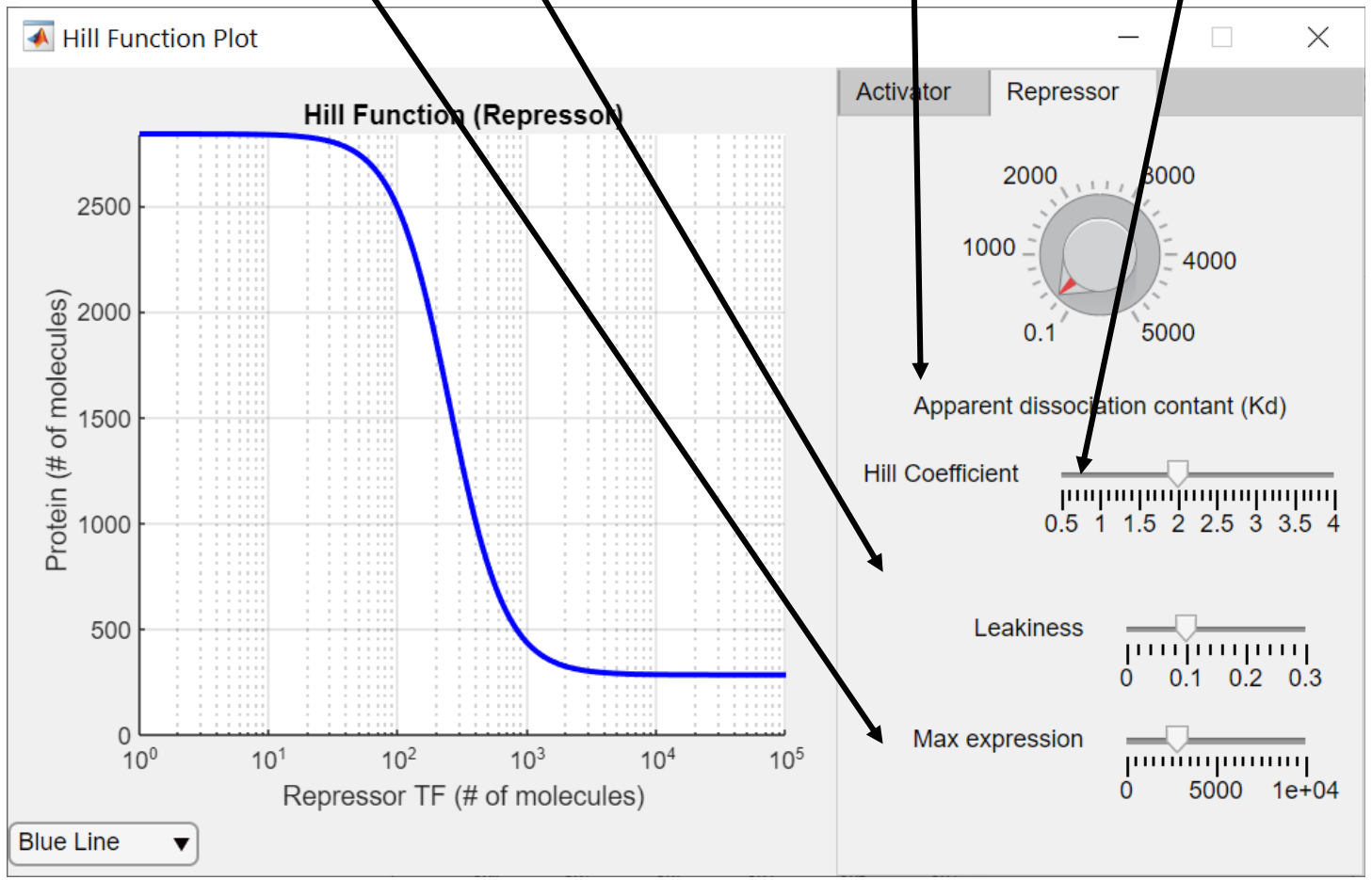
MATLAB

Gene expression regulation by Transcription Factors (TF)

Repressor

$$[\text{Protein}] = \alpha_{max}\left(\beta_0 + (1-\beta_0)\frac{K_d}{K_d + [\text{TF}]^n}\right)$$

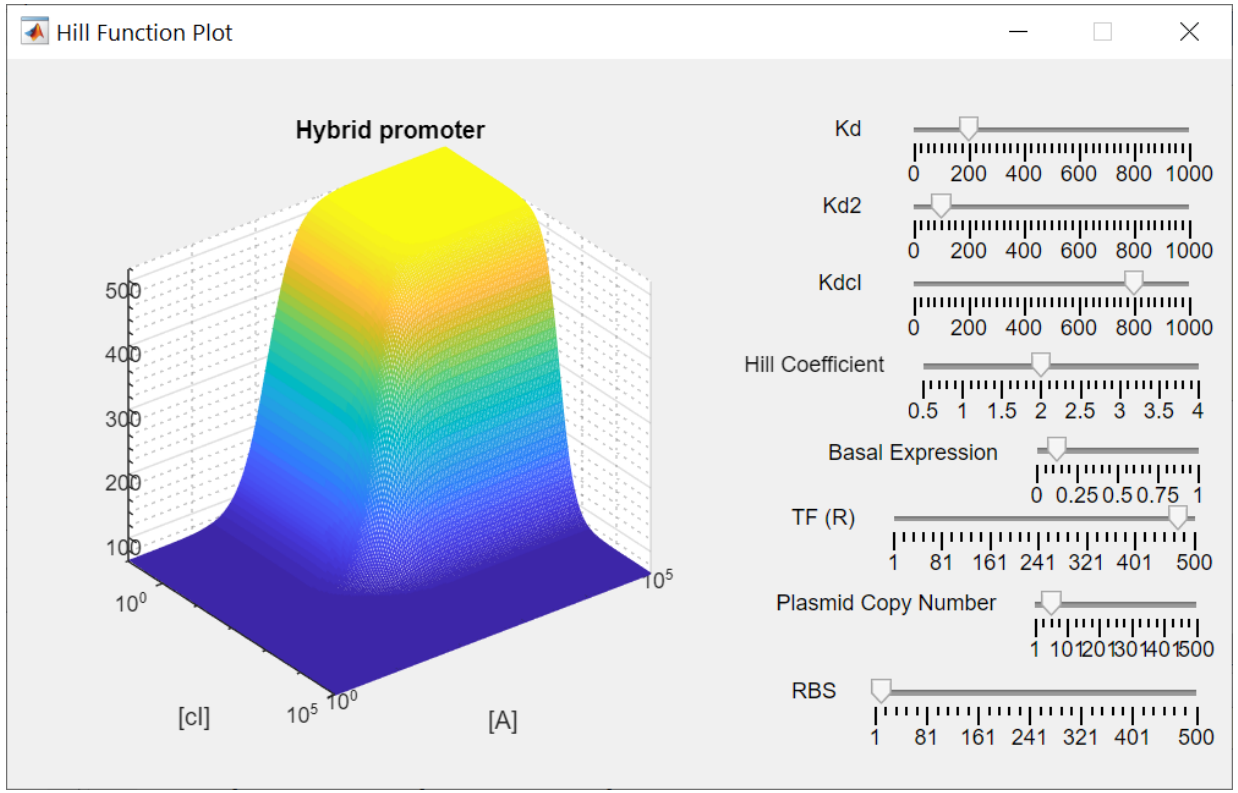
$$\alpha_{max} = k_2 \frac{k_1}{d_1 d_2} C_N$$



Gene expression regulation by Transcription Factors (TF)

Hybrid promoter

$$[\text{Protein}] = \alpha_{max}\left(\beta_0 + (1-\beta_0)\frac{\frac{1}{k_{dlux}}\left(\frac{[R][A]}{k_{d2}C_N}\right)^2}{1+\frac{1}{k_{dlux}}\left(\frac{[R][A]}{k_{d2}C_N}\right)^2}\frac{1}{1+\frac{[cI]^2}{k_{dcI}C_N}}\right)$$



Follow-up questions?

- After the seminar, ask us questions over on StackExchange!
- Bring your biology questions to: https://biology.stackexchange.com/
- Bioinformatics questions may be better on: https://bioinformatics.stackexchange.com/
- Get help with the websites at: https://2021.igem.org/Engineering/StackExchange and on slack in #stackexchange
- or contact me by email (vignoni@isa.upv.es)

Next modeling webinar -> Webinar 5:

Modeling circuits with ODEs and experimental data, stay tuned!

Go check out the Engineering Hub! https://2021.igem.org/Engineering

Thank You & Have an Exceptional Year of iGEM!