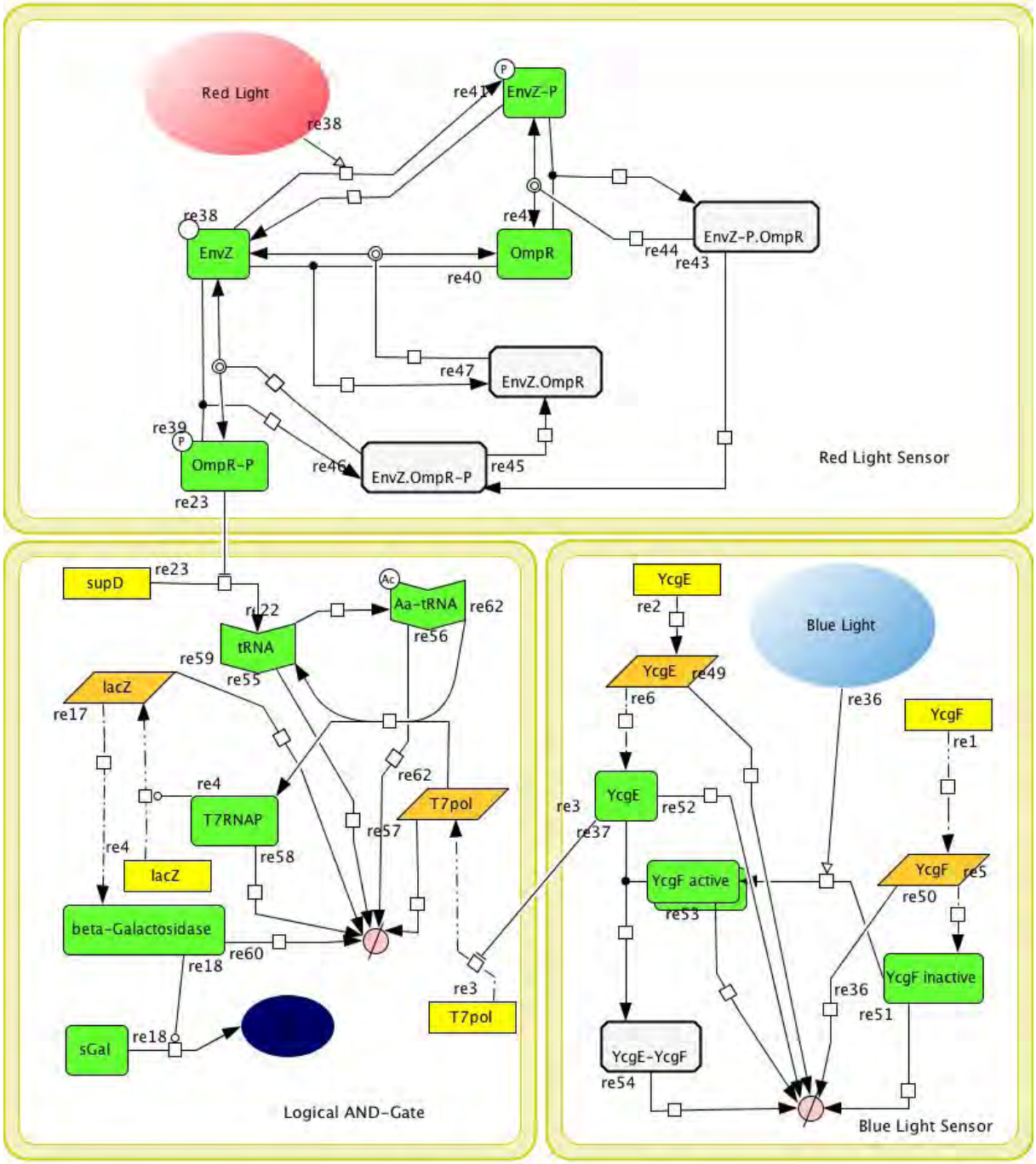
Contents

1. Model

This model combines the work previously done for the red light sensor, the blue light sensor and the AND-Gate. See the respective pages for more details


Red Light
re38
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Blue Light Sensor

2. Equations

$$
\begin{aligned}
EnvZ & \quad \dot{x}_1 = k_{ad}x_2 - k_{ap}x_1RL + k_{d2}x_4 - k_{b2}x_5x_1 - k_{b3} * x_6x_1 + k_{d3}x_7 \\
EnvZ - P & \quad \dot{x}_2 = k_{ap}x_1RL - k_{ad}x_2 + k_{d1}x_3 - k_{b1}x_6x_2 \\
EnvZ - P.OmpR & \quad \dot{x}_3 = -(k_{d1} + k_{pt})x_3 + k_{b1}x_6x_2 \\
EnvZ.OmpR - P & \quad \dot{x}_4 = k_{pt}x_3 - (k_{ph} + k_{d2})x_4 + k_{b2}x_5x_1 \\
OmpR - P & \quad \dot{x}_5 = k_{d2}x_4 - k_{b2}x_5x_1 \\
OmpR & \quad \dot{x}_6 = k_{d1}x_3 + k_{d3}x_7 - k_{b3}x_6x_1 - k_{b1}x_6x_2 \\
EnvZ.OmpR & \quad \dot{x}_7 = k_{ph}x_4 - k_{d3}x_7 + k_{b3}x_6x_1 \\
YcgF_{mRNA} & \quad \dot{x}_8 = k_1 - \gamma_{mRNA}x_8 \\
YcgF_{inactive} & \quad \dot{x}_9 = k_3x_8 - 2k_{dim}x_9^2\frac{BL^2}{\left(\frac{1}{2}+BL\right)^2} + 2k_{dis}x_{10} - \gamma_{Protein}x_9 \\
YcgF_{dimer} & \quad \dot{x}_{10} = 2k_{dim}x_9^2\frac{BL^2}{\left(\frac{1}{2}+BL\right)^2} - k_{bind}x_{10}x_{12} - k_{dis}x_{10} + k_{ubind}x_{13} - \gamma_{Protein}x_{10} \\
YcgE_{RNA} & \quad \dot{x}_{11} = k_2 - \gamma_{mRNA}x_{11} \\
YcgE_{Protein} & \quad \dot{x}_{12} = k_4x_{11} - k_{bind}x_{10}x_{12} + k_{ubind}x_{13} - \gamma_{Protein}x_{12} \\
YcgE.YcgF_{complex} & \quad \dot{x}_{13} = -k_{ubind}x_{13} + k_{bind}x_{10}x_{12} \\
tRNA & \quad \dot{x}_{14} = k_t\frac{\left(\frac{x_5}{K1}\right)^2}{\left(1+\frac{x_5}{K1}\right)^2} - (\gamma_1 + k_a)x_{14} + \gamma_{2p}x_{15} + 2k_{7p}x_{16}\left(\frac{\gamma_3}{k_{7m}}\right)\left(\frac{x_{14}}{\gamma_0+x_{14}}\right)^2 \\
Aa - tRNA & \quad \dot{x}_{15} = k_ax_{14} - 2k_{7p}x_{16}\left(\frac{\gamma_3}{k_{7m}}\right)\left(\frac{x_{14}}{\gamma_0+x_{14}}\right)^2 - \gamma_2x_{15} \\
T7RNAP_{mRNA} & \quad \dot{x}_{16} = k_{7m}\left(1 - \frac{\left(\frac{x_{12}}{K1}\right)^2}{\left(1+\frac{x_{12}}{K1}\right)^2}\right) - \gamma_3x_{16} \\
T7RNAP & \quad \dot{x}_{17} = k_{7p}x_{16}\left(\frac{\gamma_3}{k_{7m}}\right)\left(\frac{x_{14}}{\gamma_0+x_{14}}\right)^2 - \gamma_4x_{17} \\
lacZ_{mRNA} & \quad \dot{x}_{18} = \alpha_M\left(1 - \frac{\left(\frac{x_5}{K5}\right)^2}{\left(1+\frac{x_5}{K5}\right)^2}\right) - \gamma_Mx_{18} \\
\beta - Galactosidase & \quad \dot{x}_{19} = \alpha_Bx_{18} - \gamma_Bx_{19} \\
dye & \quad \dot{x}_{20} = \alpha_Ax_{19}
\end{aligned}
$$

3. Parameters

Parameter	Value	Unit	Name	Source
k_{ap}	0.1	$\frac{1}{s}$	EnvZ autophosphorelation rate	[3]
k_{ad}	0.001	$\frac{1}{s}$	EnvZ dephospholeration rate	[3]

Parameter	Value	Unit	Name	Source
k_{b1}	0.5	$\frac{1}{s}$	binding rate EnvZ-P & OmpR	[3]
k_{d1}	0.5	$\frac{1}{s}$	unbinding rate EnvZ-P.OmpR	[3]
k_{b2}	0.05	$\frac{1}{s}$	binding rate EnvZ & OmpR-P	[3]
k_{d2}	0.5	$\frac{1}{s}$	unbinding rate EnvZ.OmpR-P	[3]
k_{b3}	0.5	$\frac{1}{s}$	binding rate EnvZ & OmpR	[3]
k_{d3}	5	$\frac{1}{s}$	unbinding rate EnvZ.OmpR	[3]
k_{ph}	0.05	$\frac{1}{s}$	dephosphorelation rate EnvZ.OmpR-P	[3]
k_{pt}	1.5	$\frac{1}{s}$	phosphotransfer rate	[3]
k_1	1.54e-3	$\frac{1}{s}$	max transcription rate YcgF	[1]
k_2	0.848e-3	$\frac{1}{s}$	max transcription rate YcgE	[1]
k_3	0.167	$\frac{1}{s}$	max translation rate YcgF	[1]
k_4	0.167	$\frac{1}{s}$	max translation rate YcgE	[1]
k_{dim}	0.008	$\frac{1}{s}$	dimerization rate YcgF	[1]
k_{dis}	0.0058	$\frac{1}{s}$	dissociation rate YcgF dimer	[1]
k_{bind}	100	$\frac{1}{s}$	binding rate YcgF dimer to YcgE	[1]
k_{ubind}	1	$\frac{1}{s}$	unbinding rate YcgF.YcgE	[1]
γ_{mRNA}	2.3105e-3	$\frac{1}{s}$	degradation mRNA YcgE/YcgF	[1]
$\gamma_{Protein}$	1.9254e-5	$\frac{1}{s}$	degradation rate Protein YcgE/YcgF	[1]
k_t	$\frac{46.67}{60}$	$\frac{nM}{s}$	max transcription rate tRNA	[2]
k_a	$\frac{0.08}{60}$	$\frac{1}{s}$	synthesis rate Aa-tRNA	[2]
k_{7p}	$\frac{1.5625}{60}$	$\frac{nM}{s}$	max transcription rate T7RNAP	[2]
k_{7m}	$\frac{268*0.05}{60}$	$\frac{1}{s}$	max translation rate T7RNAP	[2]
k_S	0.3	$\frac{1}{nM}$	AND Gate rate	[2]
γ_0	1	-	threshold Aa-tRNA	guessed
γ_1	$\frac{1}{60*60}$	$\frac{1}{s}$	degradation of tRNA	[2]
γ_2	$\frac{1}{40*60}$	$\frac{1}{s}$	degradation of Aa-tRNA	[2]

Parameter	Value	Unit	Name	Source
γ_3	$\frac{1}{4.4*60}$	$\frac{1}{s}$	degradation of T7RNAP mRNA	[2]
γ_4	$\frac{46.67}{40*60}$	$\frac{1}{s}$	degradation of T7RNAP	[2]
$K1$	5	nM	response param. OmpR-P,tRNA	guessed
$K3$	600	nM	response param. YcgE,T7RNAP	guessed
$K5$	$\frac{k7p}{4*\gamma_4}$	nM	response param T7RNAP,lacZ	guessed
α_M	$\frac{0.997}{60}$	$\frac{nM}{s}$	max transcription rate lacZ	[4]
α_B	$\frac{1.661e-5}{60}$	$\frac{1}{s}$	max translation rate lacZ	[4]
α_A	$\frac{20}{60}$	$\frac{1}{s}$	enzymatic reaction rate	[4]
γ_M	$\frac{0.411}{60}$	$\frac{1}{s}$	degradation lacZ mRNA	[4]
γ_B	$\frac{8.331e-4}{60}$	$\frac{1}{s}$	degradation β-Galactosidase	[4]

4. Initial Data

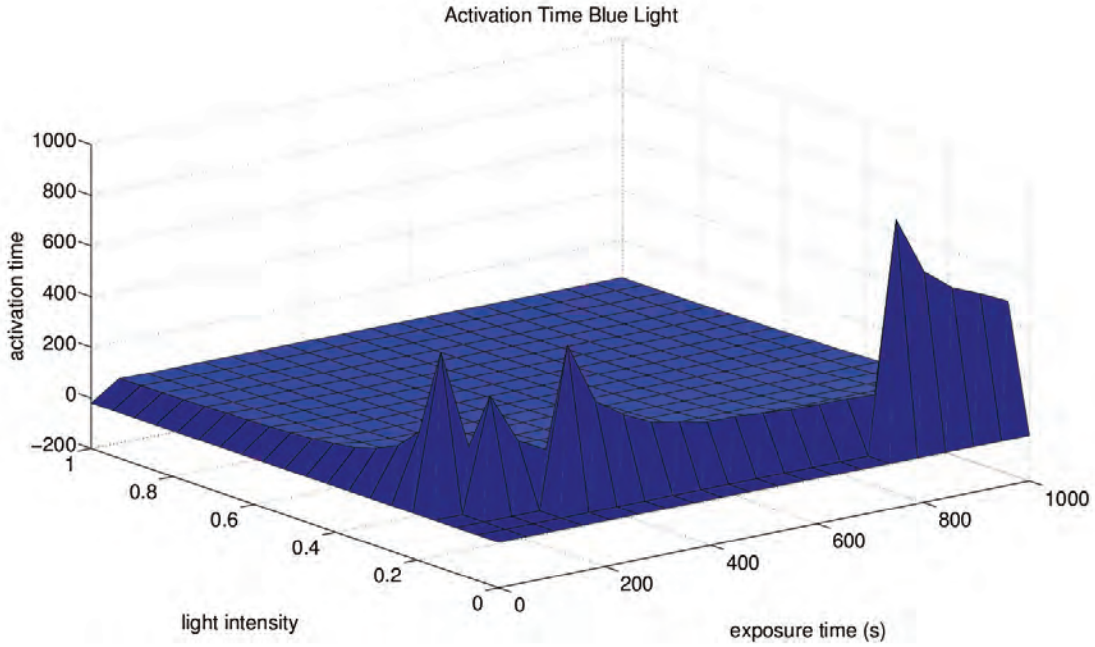
Name	Variable	Initial Value	Comment	Source
$EnvZ$	x_1	$\frac{3500}{0.60221}$	3500 molecules per cell	[3]
$EnvZ-P$	x_2	0		
$EnvZ-P.OmpR$	x_3	0		
$EnvZ.OmpR-P$	x_4	0		
$OmpR-P$	x_5	0		
$OmpR$	x_6	$\frac{100}{0.60221}$	100 molecules per cell	[3]
$EnvZ.OmpR$	x_7	0		
$YcgF_{mRNA}$	x_8	$\frac{k_1}{\gamma_{mRNA}}$	steady state	
$YcgF_{inactive}$	x_9	$\frac{k_3}{\gamma_{Protein}}\frac{k_1}{\gamma_{mRNA}}$	steady state	
$YcgF_{dimer}$	x_{10}	0		
$YcgE_{mRNA}$	x_{11}	$\frac{k_2}{\gamma_{mRNA}}$	steady state	
$YcgE$	x_{12}	$\frac{k_4}{\gamma_{Protein}}\frac{k_2}{\gamma_{mRNA}}$	steady state	
$YcgE.YcgF$	x_{13}	0		

Name	Variable	Initial Value	Comment	Source
$tRNA$	x_{14}	0		
$Aa - tRNA$	x_{15}	0		
$T7RNAP_{mRNA}$	x_{16}	0		
$T7RNAP$	x_{17}	0		
$lacZ_{mRNA}$	x_{18}	0		
$\beta - Galactosidase$	x_{19}	0		
dye	x_{20}	0		

5. Simulation

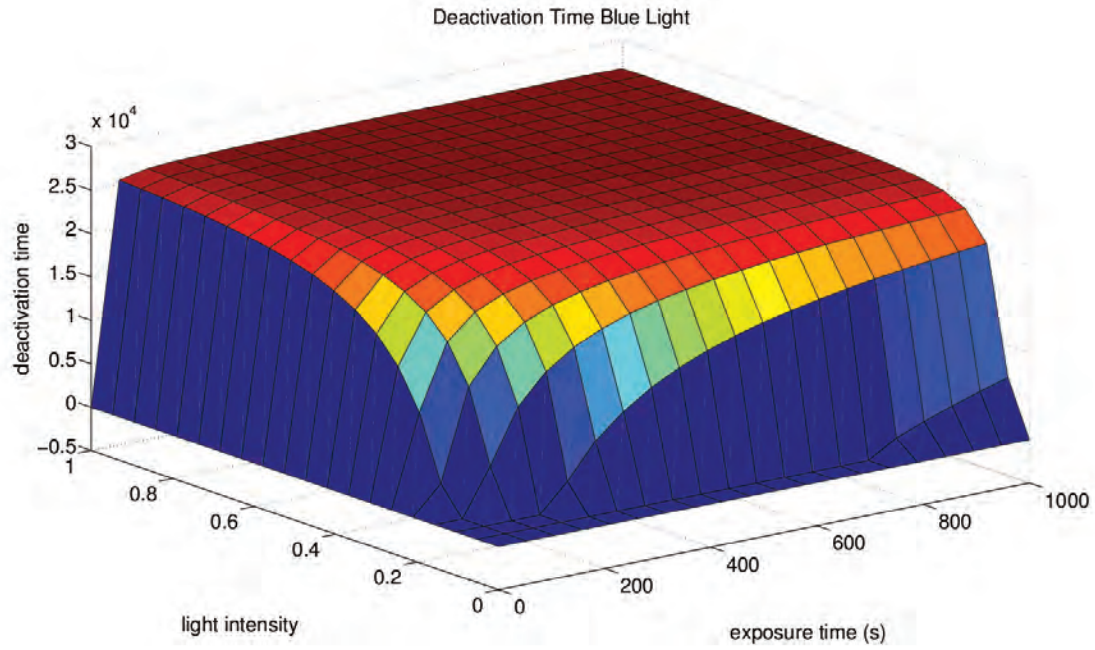
In all graphics the unit for time is seconds. Both intensities were varieed, but the intensities for blue and red light were scaled by a factor of $\frac{1}{10}$ and 10 respectively. The duration for blue light was scaled by a factor of $\frac{1}{5}$. These scaling factors were used to have vary between the same intensities and exposure times that were used in the simulation of the seperate parts. Although it would be desirable only to vary only the characteristics of the light of the wavelength that affects the corresponding part of the system, this was not done since the equations intrinsically provide that each wavelength only affects one part of the system and computations were a lot faster like this.

Firstly the activation time of the blue light sensor part was simulated since the pathway was extended by the T7 Polymerase mRNA production. The threshold for the activation was $1nM$ T7pol mRNA.



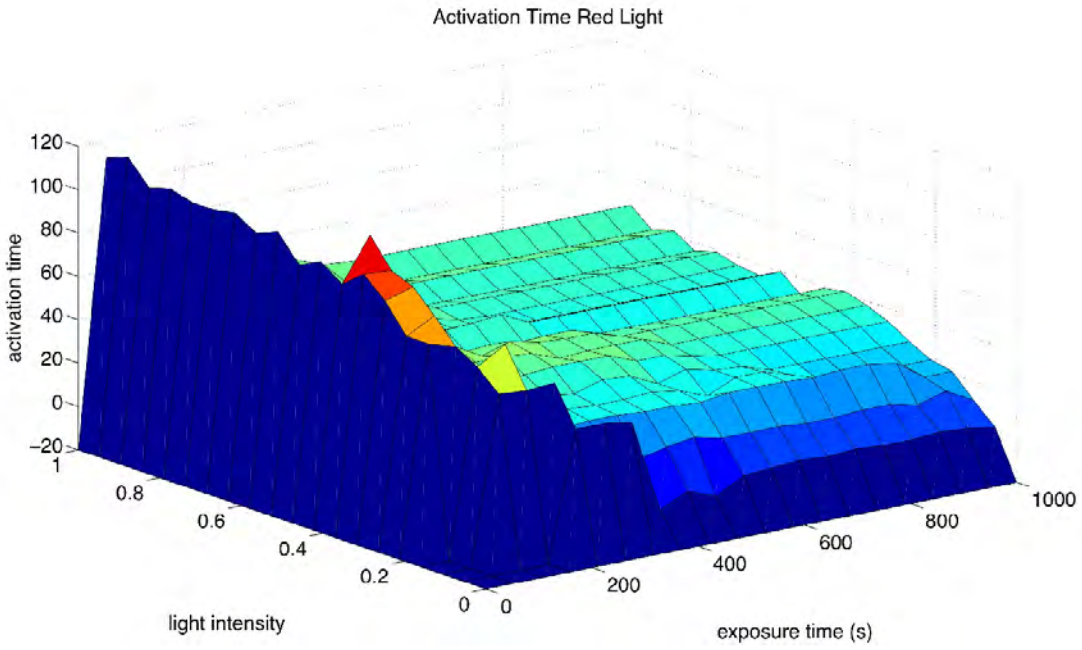
Values of -20 indicate that the threshold was not passed in the 60,000 seconds of simulation. Other values are in seconds. We see that if a minimum exposure time is exceeded the activation time only depends on the light intensity. This should coincide with real behavior. The spikes are due to numeric inaccuracies.

Secondly the deactivation time, the time at which the concentration dropped below the threshold, was simulated.

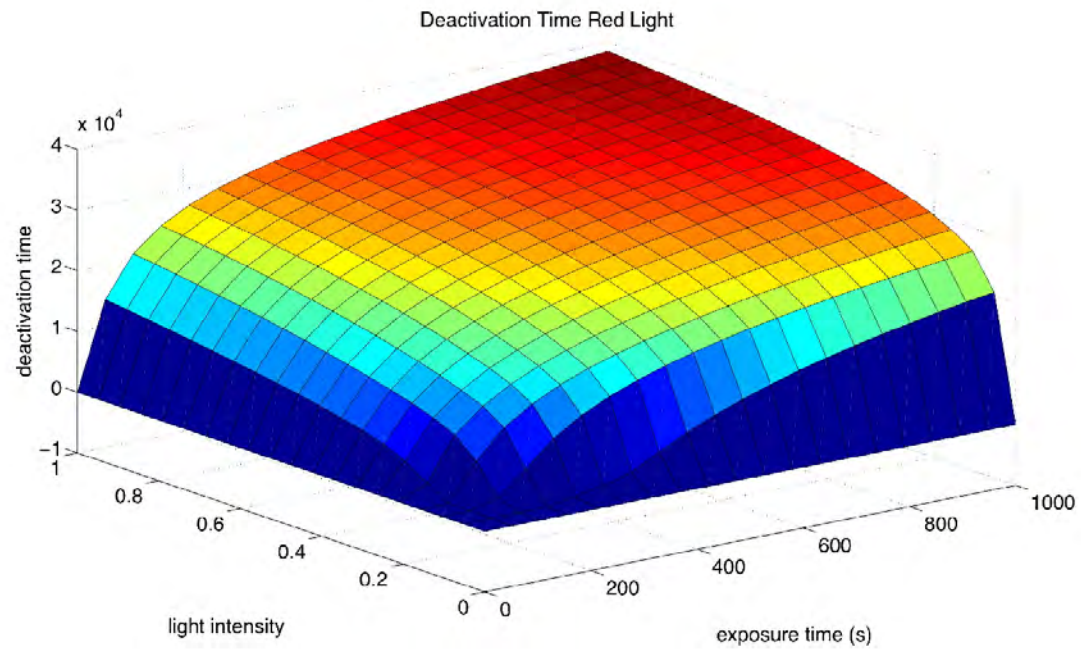


We can observe that although the deactivation time depends on both intensity and exposure time but saturates very fast with respect to both variables.

The same procedure was done for the red light sensor part. Here the concentration of tRNA served as reference and a threshold of $30nM$ was used.

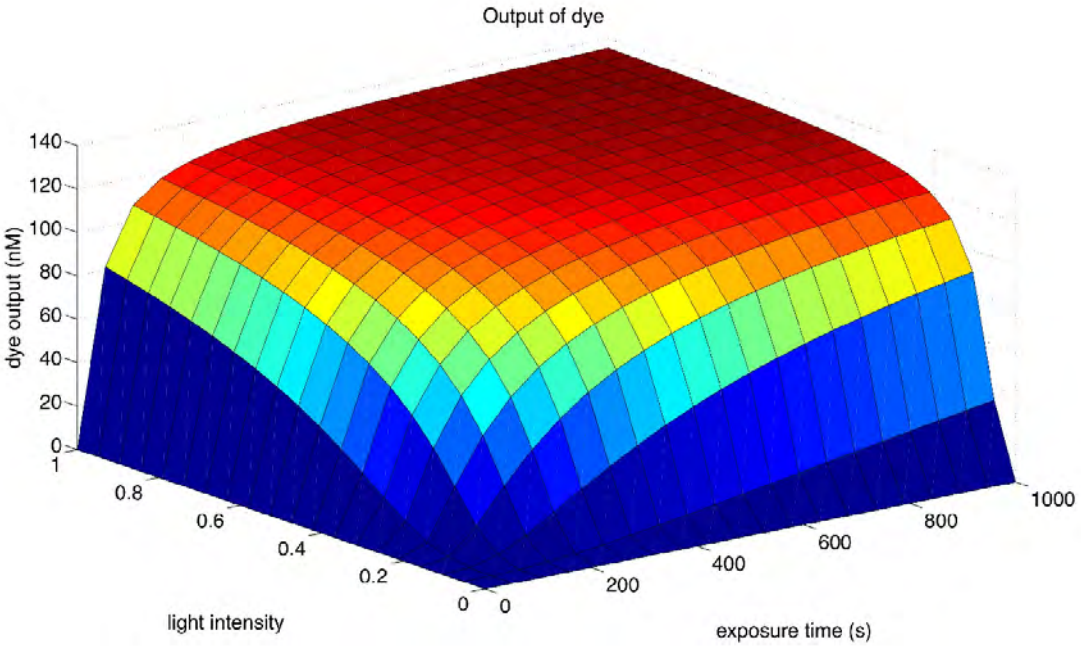


Here accurate predictions about the behavior is difficult since the values are monotonic neither in intensity nor exposure time. Still the activation time seems to be more or less independent of exposure time after a certain amount of time. The threshold is probably due to the fact that the signal needs to cascade down a pathway that involves slower reactions which dampen the signal speed if the original signal is no longer present. Wether this behavior is realistic is questionable.



The deactivation time of the red light sensor part also depends on intensity and exposure time but saturation is achieved a lot slower than for the blue light sensor part.

Finally the output of dye was simulated.



We can see that the output of dye depends on both intensity and exposure time. Of course here a simulation where both intensity and exposure time are varied independently for each wavelength would be desirable. This would mean an scaling in potency by 4 instead

of 2 in the computation time and would lead to the question how to present the data in a good fashion. Also it would be questionable wether any real information would be gained due to the inaccuracy in the parameters.

6. conclusion

All simulations should be treated with extreme care, since some parameters were only guessed and the sensitivity to errors in the guessing increases with the complexity of the whole system. Hence the results should be only used as indicator for the qualitative behavior of the system and not the quantitative behavior. Unfortunately our assays did not provide enough data to make reasonable assumptions about the missing parameters, but if this data would be available the model could also be further refined.

References

1. KU Leuven 2009, *Blue light receptor: Modeling*, 2009.
2. PKU Beijing 2009, *And gate 1*, 2009.
3. Oleg A Igoshin, Rui Alves, and Michael A Savageau, *Hysteretic and graded responses in bacterial two-component signal transduction*, Mol Microbiol **68** (2008), no. 5, 1196–215.
4. N Yildirim, M Santillan, D Horike, and MC Mackey, *Dynamics and bistability in a reduced model of the lac operon*, CHAOS **14** (2004), no. 2, 279–292 (English).