Green Sensor Modeling Abstract

Zhang Zhen

2014 年 7 月 22 日

1 Background Knowledge

1.1 Paper I

Ref: Multichromatic Control of Gene Expression in E.coli

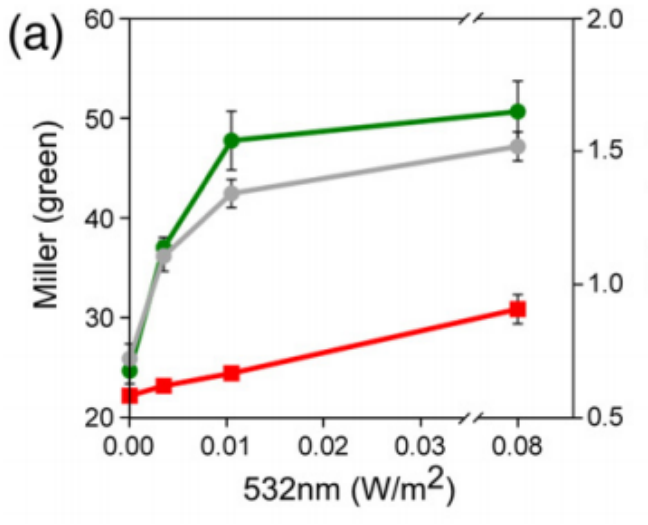
They report a green light-inducible transcription system in E.coli based on a green/red photoswitchable two-component system for cyanobacteria.

They demonstrated that the transcriptional output is proportional to the intensity of green light applied and the green sensor is orthogonal to the red sensor at intensities of 532nm light less than $0.01W/m^2$

The TCS(Two-Component-System) consists of the membrane-associated histidine CcaS and its response regulator CcaR

Absorption of green light increases the rate of CaaS autophosphorylation, phosphotransfer to CaaR, and transcription from the promoter of the phycobilisome linker protein cpcG2, while the absorption of red light reverses this process.

Here is a picture showing the relationship



1.2 Paper II

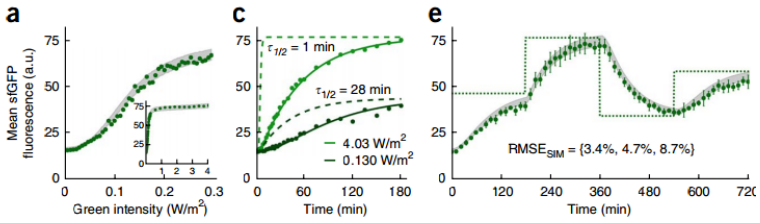
Characterizing the bacterial gene circuit dynamics with optically programmed gene expression signals

They say: In CcaS-CcaR TCS, the SK CcaS is produced in a green-absorbing ground state Pg. Absorption of green light flips CcaS to a kinase-active red-absorbing state Pr that phosphorylates the response regulator CcaR, which then binds to the cpcG2 promoter and activates transcription.

They use LTA(Light tube array) to characterize the relationship between light input and protein expression output for sensor.

Their measurements revealed that expression from CcaS-CcaR increases with green light intensity up to the LTA maximum of $4.03 W/m^2$ with a response that is fit well by a Hill function (Hill coefficient n=2.4 3.2) containing an additional linear term.

There is a nice picture illustration of their work.



My conclusion is what an awesome control!

In there paper, the downstream of PcpcG2 is tetR which deserves our attention. Their so-called function generator is actually like that: They programmed the light output of LTA, and try to output the same function with downstream expression of green sensor.

2 Modeling

2.1 Abstract

The sensor passway: light-intensity – CcaS – CcaR – Downstream Promoter cpcG2

It is a rather clear and straight line without red light. Yes, when there is red light, things get stuck.

The red light will kick CcaS Pr back to Pg, which dephos pho-CcaR, deactivating the transcription.....So we have to take red light into consideration. But let's look at their work first.

In the model of the second paper, they use two variables: sfGFP production rate $p(t)$ and sfGFP abundance $g(t)$; And three parameters:

1. short delay in response to the control signal τ_{delay}
2. light intensity dependent rate of change of the sfGFP production rate k_p
3. the sfGFP dilution rate due to cell growth k_g

Then they investigated whether the model could be used to design time-varying light programs capable of driving gene expression to follow a user-defined reference signal. The algorithm uses the dynamic model to simulate

the gene expression response and iteratively optimizes the light control program until the error between the reference and the simulation is sufficiently small.

2.2 Details

I'm not going to roll out the equation for this section, but I strongly recommend you to read further into the second paper esp. its supplementary materials.

In the paper's suits supplementary material, they give out the equation for the relationship between light intensities of green light and red light with the sfGFP production. They also give their 2D-ODE details.