Modeling the functioning of YtvA in the general stress response in Bacillus subtilis

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Supplementary Information

Modeling the functioning of YtvA in the general stress response in *Bacillus subtilis*

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Analytical approximation of the temporal changes in protein species distribution

Note that several equations from the main text are repeated in the Supplementary Information to present a coherent story. For clarity, they retain the numbering of the main text ('equation #'), while new equations are labeled 'supplementary equation #'.

Introduction

The temporal behavior of the kinetic photocycle model presented in Figure 2A can be described using three differential equations (equations 1-3). These equations can be used to simulate the temporal changes in the protein species distribution of a photoreceptor such as YtvA (Figure 2B-D; see the main text). However, for the purpose of predictions of routine experiments, differential equations can be too cumbersome. Therefore, it is of interest to obtain a simple analytical expression for the temporal changes in protein species distribution.

$$\frac{d[\mathrm{D}]}{dt} = -k_{exD}\cdot[\mathrm{D}] + \left(\frac{1}{Q_{yD}} - 1\right)\cdot k_{pe}\cdot[\mathrm{D}^*] + k_{re}\cdot[\mathrm{S}] \qquad \text{Eq. 1}$$

$$\frac{d[\mathrm{D}^*]}{dt} = k_{exD}\cdot[\mathrm{D}] - \frac{k_{pe}}{Q_{yD}}\cdot[\mathrm{D}^*] \qquad \text{Eq. 2}$$

$$\frac{d[\mathrm{S}]}{dt} = k_{pe}\cdot[\mathrm{D}^*] - k_{re}\cdot[\mathrm{S}] \qquad \text{Eq. 3}$$

Required approximations to simplify the model

To obtain such an expression, we followed a procedure analogous to the one outlined in Hendriks & Hellingwerf (2009)[1]. We assumed that the contribution of the excited state D* to the species distribution of YtvA is negligible. Our simulations with parameters for YtvA confirm that D* does not accumulate significantly (Figure 2C). This leads to supplementary equation 1, where c_{tot} represents the total concentration of the photoreceptor. In light of this, it is also reasonable to assume that the change in [D] mirrors the change in [S], as shown in supplementary equation 2.

$$c_{tot} = [\mathrm{D}] + [\mathrm{S}] \qquad \text{Supp. eq. 1}$$

$$\frac{d[\mathrm{D}]}{dt} = -\frac{d[\mathrm{S}]}{dt} \qquad \text{Supp. eq. 2}$$

Derivation of an equation for the temporal change in concentration of the dark state

Substituting equations 1 and 3 into supplementary equation 2 allows the derivation of an expression for D* in D (supplementary equation 4).

$$-k_{exD}\cdot[\mathrm{D}] + \left(\frac{1}{Q_{yD}} - 1\right)\cdot k_{pe}\cdot[\mathrm{D}^*] + k_{re}\cdot[\mathrm{S}] = -k_{pe}\cdot[\mathrm{D}^*] + k_{re}\cdot[\mathrm{S}] \qquad \text{Supp. eq. 3}$$

$$[\mathrm{D}^*] = \frac{Q_{yD}\cdot k_{exD}}{k_{pe}}\cdot[\mathrm{D}] \qquad \text{Supp. eq. 4}$$

Substituting this result and the fact that [S] is equal to c_{tot} – [D] (as follows from supplementary equation 1) into equation 1 results in supplementary equation 5, which can be rewritten to supplementary equation 6.

$$\frac{d[\mathrm{D}]}{dt} = -k_{exD} \cdot [\mathrm{D}] + \left(\frac{1}{Q_{yD}} - 1 \right) \cdot k_{pe} \cdot \frac{Q_{yD} \cdot k_{exD}}{k_{pe}} \cdot [\mathrm{D}] + k_{re} \cdot (c_{tot} - [\mathrm{D}]) \qquad \text{Supp. eq. 5}$$

$$\frac{d[\mathrm{D}]}{dt} = \alpha \cdot [\mathrm{D}] + k_{re} \cdot c_{tot} \text{ with } \alpha = -(Q_{yD} \cdot k_{exD} + k_{re}) \qquad \text{Supp. eq. 6}$$

This equation can be rewritten and integrated to obtain a solution for [D]. Note that this uses the same assumption that k_{exD} is independent of [D] as was made for the derivation of the analytical equations for the steady-state fractions (see the main text and in particular equation 4).

$$\frac{d[\mathrm{D}]}{dt} = \alpha \cdot \left([\mathrm{D}] + \frac{k_{re} \cdot c_{tot}}{\alpha} \right) \qquad \text{Supp. eq. 7}$$

$$\frac{1}{[\mathrm{D}] + \frac{k_{re} \cdot c_{tot}}{\alpha}} d[\mathrm{D}] = \alpha \, dt \quad \Rightarrow \quad \int_{[\mathrm{D}]_0}^{[\mathrm{D}]} \frac{1}{[\mathrm{D}] + \frac{k_{re} \cdot c_{tot}}{\alpha}} d[\mathrm{D}] = \alpha \cdot \int_0^t dt \qquad \text{Supp. eq. 8}$$

$$\frac{[\mathrm{D}] + \frac{k_{re} \cdot c_{tot}}{\alpha}}{[\mathrm{D}]_0 + \frac{k_{re} \cdot c_{tot}}{\alpha}} = e^{\alpha \cdot t} \qquad \text{Supp. eq. 9}$$

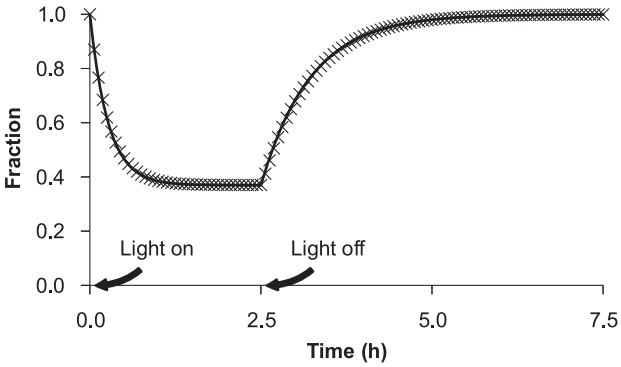
$$[\mathrm{D}] = \left([\mathrm{D}]_0 - \frac{k_{re} \cdot c_{tot}}{Q_{yD} \cdot k_{exD} + k_{re}} \right) \cdot e^{-(Q_{yD} \cdot k_{exD} + k_{re})t} + \frac{k_{re} \cdot c_{tot}}{Q_{yD} \cdot k_{exD} + k_{re}} \qquad \text{Supp. eq. 10}$$

Herein, $[\mathrm{D}]_0$ represents the starting concentration of the protein in the dark state. The fraction of the protein in the dark state can easily be derived from supplementary equation 10.

$$f_D = \frac{[\mathrm{D}]}{c_{tot}} = \left(\frac{[\mathrm{D}]_0}{c_{tot}} - \frac{k_{re}}{Q_{yD} \cdot k_{exD} + k_{re}} \right) \cdot e^{-(Q_{yD} \cdot k_{exD} + k_{re})t} + \frac{k_{re}}{Q_{yD} \cdot k_{exD} + k_{re}} \qquad \text{Eq. 30}$$

If the time is set to infinite in equation 30, the exponential part of the equation is canceled, and the equation simplifies to the steady-state equation for the fraction of protein in the dark state (equation 28), as expected.

Using the same parameters for YtvA as used in Figure 2, we compared the outcome of equation 30 (solid line in Supplementary Figure 1) to simulations with the differential equations (crosses). Both simulations overlap, verifying the validity of the assumptions.



Supplementary Figure 1. Comparison of the fraction of the protein in the dark state as calculated with the analytical approximation (equation 30; solid line, no symbols), and via a simulation with the differential equations 1-3 (crosses, no line), using the same parameters as in Figure 2. In the simulation, a light from the same source as in Figure 2 with intensity 1 µEinstein · m^{-2} · s^{-1} was turned on at time point zero. After 2.5 hours, the light was turned off again.

Derivation of an equation for the time needed to reach a given percentage of steady state

Another interesting application of equation 30 is in rewriting it to obtain an expression for the time it takes before a certain percentage of steady state is reached. If $f_{\text{steady state}}$ is taken to be the fraction (between 0 and 1) of the change in response to the given perturbation in light intensity that has taken place, then the relationship in supplementary equation 11 holds.

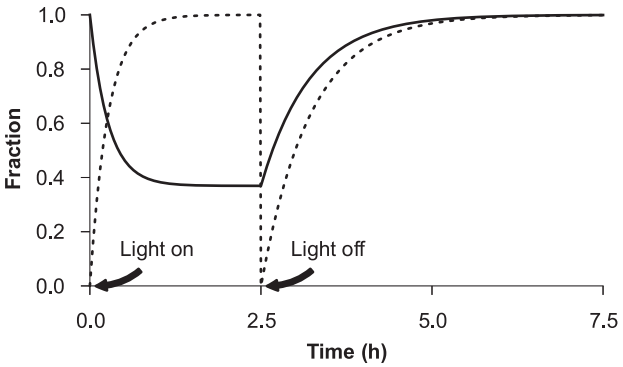
$$f_{\text{steady state}} = 1 - e^{-\left(Q_{yD} \cdot k_{exD} + k_{re}\right)t} \qquad \text{Supp. eq. 11}$$

This can be rewritten to obtain equation 31.

$$\ln\left(1 - f_{\text{steady state}}\right) = -\left(Q_{yD} \cdot k_{exD} + k_{re}\right) \cdot t \qquad \text{Supp. eq. 12}$$

$$t = \frac{\ln\left(1 - f_{\text{steady state}}\right)}{-\left(Q_{yD} \cdot k_{exD} + k_{re}\right)} \qquad \text{Eq. 31}$$

It is important to note that $f_{\text{steady state}}$ represents the fraction of the change in f_D that will take place as a result of the perturbation in light intensity. Thus, an $f_{\text{steady state}}$ of 0.95 is equal to 0.95 · Δf_D (see Supplementary Figure 2). It should also be noted that it is not possible to use this formula to calculate the time it takes to reach steady state, as a true steady state takes an infinite time to reach.



Supplementary Figure 2. Illustration of the value of $f_{\text{steady state}}$ in the same simulation as in Supplementary Figure 1. The solid line is the same as in Supplementary Figure 1 (the result of applying equation 30), while the dotted line represents the value of $f_{\text{steady state}}$.

Supplementary References

1 J. Hendriks and K. J. Hellingwerf, *J. Biol. Chem.,* 2009, **284**, 5277-5288 (DOI:10.1074/jbc.M805904200).