# Models

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## 1 Iteration 1

Iteration 1 refers to the first set of the models which describe the full model as decided by the drylab. This version has subsequentially been altered as documentated in the following sections.

### 1.1 Full Model with mRNA - F1

$$\dot{TFS} = \beta_{TFS}\frac{s}{\gamma_{TFS}+s} - k_d TFS \quad (1)$$

$$\dot{s} = -\delta_s s - \beta_{TFS}\frac{s}{\gamma_{TFS}+s} + k_d TFS \quad (2)$$

$$\dot{mRNA}_{PhzM} = \beta_{mRNA_{PhzM}}\frac{TFS}{\gamma_{mRNA_{PhzM}}+TFS} - \delta_{mRNA_{PhzM}} mRNA_{PhzM} \quad (3)$$

$$\dot{mRNA}_{PhzS} = \beta_{mRNA_{PhzS}}\frac{TFS}{\gamma_{mRNA_{PhzS}}+TFS} - \delta_{mRNA_{PhzS}} mRNA_{PhzS} \quad (4)$$

$$\dot{PhzM} = \lambda_{PhzM} mRNA_{PhzM} - \delta_{PhzM} PhzM \quad (5)$$

$$\dot{PhzS} = \lambda_{PhzS} mRNA_{PhzS} - \delta_{PhzS} PhzS \quad (6)$$

$$\dot{MPCAB} = \beta_{MPCAB}\frac{PhzM}{\gamma_{MPCAB}+PhzM} - \delta_{MPCAB} MPCAB - \beta_{PYO}\frac{MPCAB}{(\gamma_{PYO_{MPCAB}}+MPACB)}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} \quad (7)$$

$$\dot{PYO} = \beta_{PYO}\frac{MPCAB}{(\gamma_{PYO_{MPCAB}}+MPACB)}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} - \delta_{PYO} PYO \quad (8)$$

## 1.2 Full Model without mRNA - F2

$$\dot{TFS} = \beta_{TFS}\frac{s}{\gamma_{TFS}+s} - k_d TFS \tag{9}$$

$$\dot{s} = -\delta_s s - \beta_{TFS}\frac{s}{\gamma_{TFS}+s} + k_d TFS \tag{10}$$

$$\dot{PhzM} = \beta_{PhzM}\frac{TFS}{\gamma_{PhzM}+TFS} - \delta_{PhzM} PhzM \tag{11}$$

$$\dot{PhzS} = \beta_{PhzS}\frac{TFS}{\gamma_{PhzS}+TFS} - \delta_{PhzS} PhzS \tag{12}$$

$$\dot{MPCAB} = \beta_{MPCAB}\frac{PhzM}{\gamma_{MPCAB}+PhzM} - \delta_{MPCAB} MPCAB - \beta_{PYO}\frac{MPCAB}{(\gamma_{PYO_{MPCAB}}+MPACB)}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} \tag{13}$$

$$\dot{PYO} = \beta_{PYO}\frac{MPCAB}{(\gamma_{PYO_{MPCAB}}+MPACB)}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} - \delta_{PYO} PYO \tag{14}$$

## 1.3 Positive Feedback Loop (without mRNA) - F3

$$\dot{TF} = \alpha_{TF} + \beta_{TF}\frac{TFS}{\gamma_{TF}+TFS} - \delta_{TF} TF \tag{15}$$

$$\dot{TFS} = \beta_{TFS}\frac{s}{(\gamma_{TFS_s}+s)}\frac{TF}{(\gamma_{TFS_{TF}}+TF)} - k_d TFS \tag{16}$$

$$\dot{s} = -\delta_s s - \beta_{TFS}\frac{s}{(\gamma_{TFS_s}+s)}\frac{TF}{(\gamma_{TFS_{TF}}+TF)} + k_d TFS \tag{17}$$

$$\dot{PhzM} = \beta_{PhzM}\frac{TFS}{\gamma_{PhzM}+TFS} - \delta_{PhzM} PhzM \tag{18}$$

$$\dot{PhzS} = \beta_{PhzS}\frac{TFS}{\gamma_{PhzS}+TFS} - \delta_{PhzS} PhzS \tag{19}$$

$$\dot{MPCAB} = \beta_{MPCAB}\frac{PhzM}{\gamma_{MPCAB}+PhzM} - \delta_{MPCAB} MPCAB - \beta_{PYO}\frac{MPCAB}{(\gamma_{PYO_{MPCAB}}+MPACB)}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} \tag{20}$$

$$\dot{PYO} = \beta_{PYO}\frac{MPCAB}{(\gamma_{PYO_{MPCAB}}+MPACB)}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} - \delta_{PYO} PYO \tag{21}$$

## 1.4 Constitutive Expression Of PhzM (without mRNA) - F4

$$\dot{TFS} = \beta_{TFS}\frac{s}{\gamma_{TFS}+s} - k_d TFS \tag{22}$$

$$\dot{s} = -\delta_s s - \beta_{TFS}\frac{s}{\gamma_{TFS}+s} + k_d TFS \tag{23}$$

$$\dot{PhzS} = \beta_{PhzS_1}\frac{TFS}{\gamma_{PhzS_1}+TFS} - \delta_{PhzS} PhzS \tag{24}$$

$$\dot{PYO} = \beta_{PYO_{PhzS}}\frac{PhzS}{(\gamma_{PYO_{PhzS}}+PhzS)} - \delta_{PYO} PYO \tag{25}$$

## 1.5 Constraints

$$\beta_{PhzS_1} > \beta_{PhzS} \tag{26}$$

$$\gamma_{PhzS_1} > \gamma_{PhzS}$$

## 1.6 Constants Canon

| *No* | *name* | *value* |
|---|---|---|
| 1 | beta_TFS | |
| 2 | gamma_TFS | |
| 3 | kd | |
| 4 | delta_s | |
| 5 | beta_mRNA_PhzM | |
| 6 | gamma_mRNA_PhzM | |
| 7 | delta_mRNA_PhzM | |
| 8 | beta_mRNA_PhzS | |
| 9 | gamma_mRNA_PhzS | |
| 10 | delta_mRNA_PhzS | |
| 11 | lambda_PhzM | |
| 12 | delta_PhzM | |
| 13 | lambda_PhzS | |
| 14 | delta_PhzS | |
| 15 | beta_MPCAB | |
| 16 | gamma_MPCAB | |
| 17 | delta_MPCAB | |
| 18 | beta_PYO | |
| 19 | gamma_PYO_MPCAB | |
| 20 | gamma_PYO_PhzS | |
| 21 | delta_PYO | |
| 22 | beta_PhzM | |
| 23 | gamma_PhzM | |
| 24 | beta_PhzS | |
| 25 | gamma_PhzS | |
| 26 | alpha_TF | |
| 27 | beta_TF | |
| 28 | gamma_TF | |
| 29 | gamma_TFS_s | |
| 30 | gamma_TFS_TF | |
| 31 | beta_PhzS_1 | |
| 32 | gamma_PhzS_1 | |
| 33 | beta_PYO_PhzS | |
| 34 | gamma_PYO_PhzS | |
| 35 | delta_TF | |

# 2 Iteration 2

Iteration 2 is a further development and refinement of Iteration 1. The key changes in Iteration 2 are described and explained below.

1. Firstly the differential of the signal has been removed. This was due to deciding that the behaviour of the system would not be changed significantly by the change in the signal.
2. Next the production of MPCAB has also been dropped, this was on the advice of David Leader [2]. It was discovered that the behaviour of PhzM and PhzS are interdependant and cannot be easily seperated. The result is that the PhzM and PhzS are combined in Iteration 2.
3. It was also decided to not include mRNA in Iteration 2. This will hopefully simplify the model.

**More comments need to be added here!**

## 2.1 No feedback loops - F5

$$\dot{TF} = \alpha_{TF} - \delta_{TF}TF - \beta_{TFS}\frac{s}{(\gamma_{TFS}+s)}TF + k_dTFS \tag{27}$$

$$\dot{TFS} = \beta_{TFS}\frac{s}{(\gamma_{TFS}+s)}TF - k_dTFS - \delta_{TFS}TFS \tag{28}$$

$$\dot{PhzMS} = \beta_{PhzMS}\frac{TFS}{\gamma_{PhzMS}+TFS} - \delta_{PhzMS}PhzMS \tag{29}$$

$$\dot{PYO} = \alpha_{PYO}PhzMS - \delta_{PYO}PYO \tag{30}$$

## 2.2 With positive feedback loop - F6

In model F6 we add a term of $\beta_{TF}\frac{TFS}{\gamma_{TF}+TFS}$ to $\dot{TF}$ this represents the additional production of $TF$.

$$\dot{TF} = \alpha_{TF} + \beta_{TF}\frac{TFS}{\gamma_{TF}+TFS} - \delta_{TF}TF \tag{31}$$

$$\dot{TFS} = \beta_{TFS}\frac{s}{(\gamma_{TFS}+s)}TF - k_dTFS - \delta_{TFS}TFS \tag{32}$$

$$\dot{PhzMS} = \beta_{PhzMS}\frac{TFS}{\gamma_{PhzMS}+TFS} - \delta_{PhzMS}PhzMS \tag{33}$$

$$\dot{PYO} = \alpha_{PYO}PhzMS - \delta_{PYO}PYO \tag{34}$$

### 2.3 Constant Canon

| *No* | *name* | *value* | *range* | *reference* |
|---|---|---|---|---|
| 1 | s | | | |
| 2 | alpha_TF | | | |
| 3 | delta_TF | $3.8508e-4s^{-1}$ | $5.7762e-4-2.5672e-4$ | |
| 4 | beta_TFS | $10^6 s^{-1}$ | | |
| 5 | gamma_TFS | $4\mu M$ | | |
| 6 | delta_TFS | $3.8508e-4s^{-1}$ | $5.7762e-4-2.5672e-4$ | |
| 7 | kd | | | |
| 8 | beta_PhzMS | $0.1s^{-1}$ | | |
| 9 | gamma_PhzMS | $5\mu M$ | $0.1-10$ | |
| 10 | delta_PhzMS | $8.0225e-6s^{-1}$ | | |
| 11 | alpha_PYO | $1.3s^{-1}$ | | |
| 12 | delta_PYO | $1.6045e-5s^{-1}$ | | human cells [1] |
| 13 | beta_TF | | | |
| 14 | gamma_TF | | | |

# References


[1] Yunxia Q. O'Malley, Maher Y. Abdalla, Michael L. McCormick, Krzysztof J. Reszka, Gerene M. Denning, and Bradley E. Britigan. Subcellular localization of Pseudomonas pyocyanin cytotoxicity in human lung epithelial cells. *Am J Physiol Lung Cell Mol Physiol*, 284(2):L420–430, 2003.

[2] J. Parsons, B. Greenhagen, K. Shi, K. Calabrese, H. Robinson, and J. Ladner. Structural and functional analysis of the pyocyanin biosynthetic protein phzm from pseudomonas aeruginosa. *Biochemistry*, 2007.