Mathematical model for biofuel

The model consists of five ordinary differential equations:

$$\frac{dn(t)}{dt} = \alpha_n\, n(t)\,(1 - n(t)) - \delta_n\, b_i(t)\, n(t) - \frac{\alpha_n\, n(t)\, p(t)}{p(t) + \gamma_p} \quad (1)$$

$$\frac{dR(t)}{dt} = \alpha_R + k_R\, \frac{I}{I + \gamma_I} - \beta_R\, R(t) \quad (2)$$

$$\frac{dp(t)}{dt} = \alpha_P + k_p\, \frac{1}{\frac{R(t)}{1 + k_b\, b_i(t)} + \gamma_R} - \beta_p\, p(t) \quad (3)$$

$$\frac{db_i(t)}{dt} = \alpha_b\, n(t) - \delta_b\, p(t)\, b_i(t) \quad (4)$$

$$\frac{db_e(t)}{dt} = V\, \delta_b\, p(t)\, b_i(t)\, n(t) \quad (5)$$

Some intuitive explanations of (some of) these equations can be found towards the end of this document.

Note that for the purpose of simulation, there are three groups of quantities:

1. Time dependent variables: n(t), p(t), R(t), b_i(t) and b_e(t). These are quantities that you want to use simulation to obtain.
2. Two design parameters: α_b (Python variable: alpha_b) and α_p (Python variable: alpha_p). You will use different values of these two parameters in simulation to see how they change the amount of fuel produced internally and externally. Note that alpha_b and alpha_p are two inputs to the simulation function that you need to write.
3. The rest of the parameters (α_n, δ_n etc.) are constants. A mapping between the mathematical symbols and their Python constant names is provided below. You will need to make use of these constants in your Python simulation code. Essentially, you replace the mathematical symbol by its corresponding Python name in your simulation code.

Mapping between symbol names and Python constant names

The Python constant names are in upper case. For most symbols, the first part is the name of the Greek alphabet, followed by an underscore and then the subscript. The values of these constants are defined in the file biofuel_system_parameter_sets.py.

Symbol in equations	Constants in Python	Meaning
α_n	ALPHA_N	Cell growth rate
α_R	ALPHA_R	Basal repressor production rate
β_R	BETA_R	Repressor degradation rate
β_p	BETA_P	Pump degradation rate
δ_n	DELTA_N	Biofuel toxicity coefficient
δ_b	DELTA_B	Biofuel export rate per pump
γ_p	GAMMA_P	Pump toxicity threshold
γ_I	GAMMA_I	Inducer saturation threshold
γ_R	GAMMA_R	Repressor saturation threshold
k_R	K_R	Repressor activation constant
k_p	K_P	Pump activation constant
k_b	K_B	Repressor deactivation constant
V	V	Ratio of intra to extracellular volume
I	I	Amount of inducer

Euler's forward method

The next step is to apply Euler's forward method to the ordinary differential equations, which result in the following equations you need for simulation:

$$
\begin{aligned}
n(t+\Delta) &= n(t) + \left(\alpha_n\, n(t)\,(1-n(t)) - \delta_n\, b_i(t)\, n(t) - \frac{\alpha_n\, n(t)\, p(t)}{p(t)+\gamma_p}\right)\Delta \\
R(t+\Delta) &= R(t) + \left(\alpha_R + k_R\,\frac{I}{I+\gamma_I} - \beta_R\, R(t)\right)\Delta \\
p(t+\Delta) &= p(t) + \left(\alpha_P + k_p\,\frac{1}{\frac{R(t)}{1+k_b\, b_i(t)} + \gamma_R} - \beta_p\, p(t)\right)\Delta \\
b_i(t+\Delta) &= b_i(t) + \left(\alpha_b\, n(t) - \delta_b\, p(t)\, b_i(t)\right)\Delta \\
b_e(t+\Delta) &= b_e(t) + \left(V\,\delta_b\, p(t)\, b_i(t)\, n(t)\right)\Delta
\end{aligned}
$$

Meaning behind the equations

Right-hand side (RHS) of (1) describes the rate of change in the amount of bacteria. The first term is the logistic growth function taking into account the limitation of resources. You can learn more on logistic growth from this Wikipedia page (https://en.wikipedia.org/wiki/Logistic_function). The second term is the death rate of bacteria due to biofuel. The third term is the death rate due to efflux pumps.

RHS of (3) is the rate of change in the number of efflux pumps. The first term is a base production rate. The second term describes how biofuel in the bacteria affects the production rate. Essentially, the more the biofuel inside the bacteria, the higher the production rate. The last term is the pump degradation rate.

RHS of (4) is the rate of production of biofuel in the interior of bacteria. The first term says the production rate is proportional to the amount of bacteria. The second term is the rate at which biofuel is pumped out of the bacteria by efflux pumps.

RHS of (5) is the rate at which biofuel is pumped into the exterior.