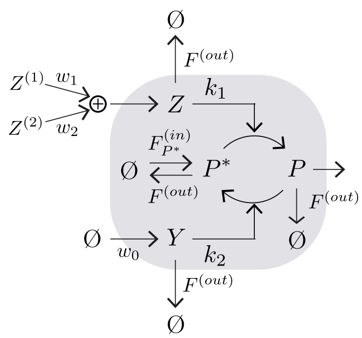
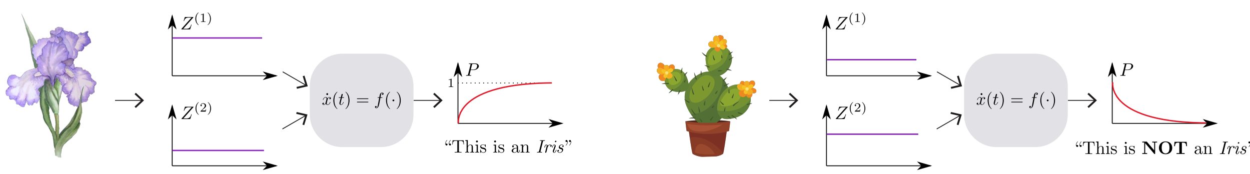
CHEM-E7225/2022: Exercise 03

Task 1 (Learning for Biochemical Neural Networks).
Consider a simplified version of the phosphorylation-dephosphorylation cycle[1] from Exercise 01 (see diagram). In this version, kinase Z is produced from two different sources $Z^{(1)}$ and $Z^{(2)}$ with production rates w_1 and w_2, respectively. As before, phosphatase Y is produced from a single source with production rate w_0. The dynamics of intermediate products (C_1, C_2) have been incorporated to the dynamics of the other components.



$$Z^{(1)} \xrightarrow{w_1} Z, \qquad Z^{(2)} \xrightarrow{w_2} Z, \qquad \emptyset \xrightarrow{w_0} Y,$$
$$Z, Y, P^* \xrightarrow{F^{(out)}} \emptyset,$$
$$Z + P^* \xrightarrow{k_1} P + Z,$$
$$Y + P \xrightarrow{k_2} P^* + Y.$$

Under this setup, this circuit corresponds to a molecular perceptron (a single-neuron neural network) capable of performing linear classification. That is, the circuit is capable to predict the category (through P) of an observation described by two variables ($Z^{(1)}$ and $Z^{(2)}$), given that the condition for belonging to a category can be represented by a linear relationship of the descriptors. As a simple example, the following diagram shows how this bio-system can classify whether a flower is an *Iris* based on the length and width of its petals



The mass balances for the individual components lead to the following nonlinear dynamics

$$\frac{d[Z^{tot}]}{dt} = (w_1 Z^{(1)} + w_2 Z^{(2)}) - F^{(out)}[Z^{tot}]; \tag{1a}$$
$$\frac{d[Y^{tot}]}{dt} = w_0 - F^{(out)}[Y^{tot}]; \tag{1b}$$
$$\frac{d[P^{tot}]}{dt} = F^{(in)}_{P^*} - F^{(out)}[P^{tot}]; \tag{1c}$$
$$\frac{d[P]}{dt} = k_1 \frac{[P^{tot}] - [P]}{[P^{tot}] - [P] + K_1}[Z^{tot}] - k_2 \frac{[P]}{[P] + K_2}[Y^{tot}]; \tag{1d}$$

The state vector is $x(t) = \big([Z^{tot}](t), [Y^{tot}](t), [P^{tot}](t), [P](t)\big)$ and the controls are $u(t) = \big(w_0(t), w_1(t), w_2(t)\big)$. The system is also subjected to a set of non-manipulated inputs, the disturbances $d(t) = \big(Z^{(1)}(t), Z^{(2)}(t)\big)$. The vector of model parameters in nominal operating conditions is the following

$$\theta_x = \Big(F^{(in)}_{P^*},\ F^{(out)},\ k_1,\ k_2,\ K_1,\ K_2\Big) = \big(1,\ 1,\ 10,\ 10,\ 0.05,\ 0.05\big)$$

[1]For more details, see *C. Cuba Samaniego, A. Moorman, G. Giordano, E. Franco*, Signaling-based neural networks for cellular computation, *bioRxiv 2020.11.10.377077, 2020*

Adapt the starting code in the archive `E3_code.zip` to solve this problem.

1. Re-write the dynamic model in Eq. (1) using the control notation as $\dot{x}(t) = f(x(t), u(t), d(t)|\theta_x)$ and implement the equations in the `biochemNN.m` file. Adapt the `E03_main.m` file to discretise the dynamics of the process using a Range-Kutta 4 (RK4) integrator with $N = 10$ steps and $\Delta t = 0.01$ units-of-time.

2. Using the `E03_main.m` template, implement the following discrete-time optimal control problem using the simultaneous approach with `CasADi/IPOPT`,

$$\min_{\substack{x_0,\dots,x_K \\ u_0,\dots,u_K}} \quad \sum_{k=0}^{K-1} \left[(x_k - x_k^{ref})^T Q (x_k - x_k^{ref}) + u_k^T R u_k \right] \tag{2a}$$

$$\text{subject to} \quad x_{k+1} - f(x_k, u_k, d_k|\theta_x) = 0, \qquad k = 0, 1, \dots, K-1 \tag{2b}$$

$$u_{k+1} - u_k = 0, \qquad k = 0, 1, \dots, K-1 \tag{2c}$$

$$x_k^{\min} \leq x_k \leq x_k^{\max}, \qquad k = 0, 1, \dots, K \tag{2d}$$

$$u_k^{\min} \leq u_k \leq u_k^{\max}, \qquad k = 0, 1, \dots, K \tag{2e}$$

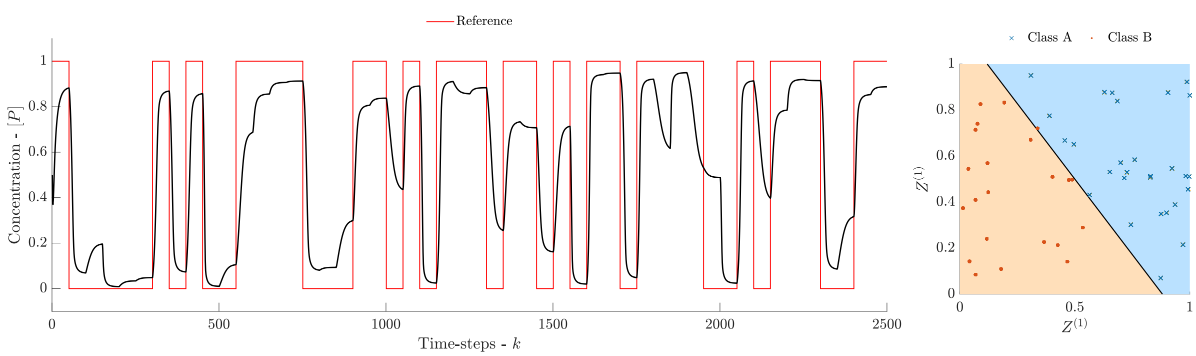
$$x_0 - \hat{x}_0 = 0. \tag{2f}$$

The input values $d_k = [Z_k^{(1)} \; Z_k^{(2)}]^T$ and state-references x_k^{ref} (for $k = 0, \dots, K$) are known and provided as data for the optimisation problem. The weighting matrices $Q \succeq 0$ and $R \succ 0$ are

$$Q = \begin{bmatrix} 0 & & & \\ & 0 & & \\ & & 0 & \\ & & & 10 \end{bmatrix}, \qquad \text{and} \qquad R = \begin{bmatrix} 10^{-3} & & \\ & 10^{-3} & \\ & & 10^{-3} \end{bmatrix}.$$

The control bounds are $u_k^{\min} = [0\;0\;0\;0]^T$ and $u_k^{\max} = [1\;1\;1\;1]^T$, for all $k = 0, \dots, K$. The state-vector is constrained to be positive, that is, $x_k^{\min} = [0\;0\;0\;0]^T$ and $x_k^{\max} = [\infty\;\infty\;\infty\;\infty]^T$, for all $k = 0, \dots, K$. The initial state is $\hat{x}_0 = [0.5\;0.5\;0.5\;0.5]^T$. Consider a horizon of $K = 2500$ time-steps.

Plot the results using the plotting functions provided in the script. Try different (but feasible) initial solutions. If correct, your solution will return figures similar (not necessarily identical) to the following



3. Comment on the results of the optimisation (*number of iterations, execution time, etc*).