Engineering associative learning in multicellular microbial consortia

Supplementary Information

Javier Macia[1,2], Blai Vidiella[1,2], Ricard Solé[1,2,3,*]

1. ICREA-Complex Systems Lab, Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Dr. Aiguader 88, 08003 Barcelona, Spain

2. Institut de Biologia Evolutiva (CSIC-Universitat Pompeu Fabra), Passeig Maritim de la Barceloneta 37, 08003 Barcelona, Spain

3. Santa Fe Institute, 1399 Hyde Park Road, Santa Fe, NM 87501, USA

∗ corresponding author

Contents

1. ISOLATED CELLS TIME SERIES

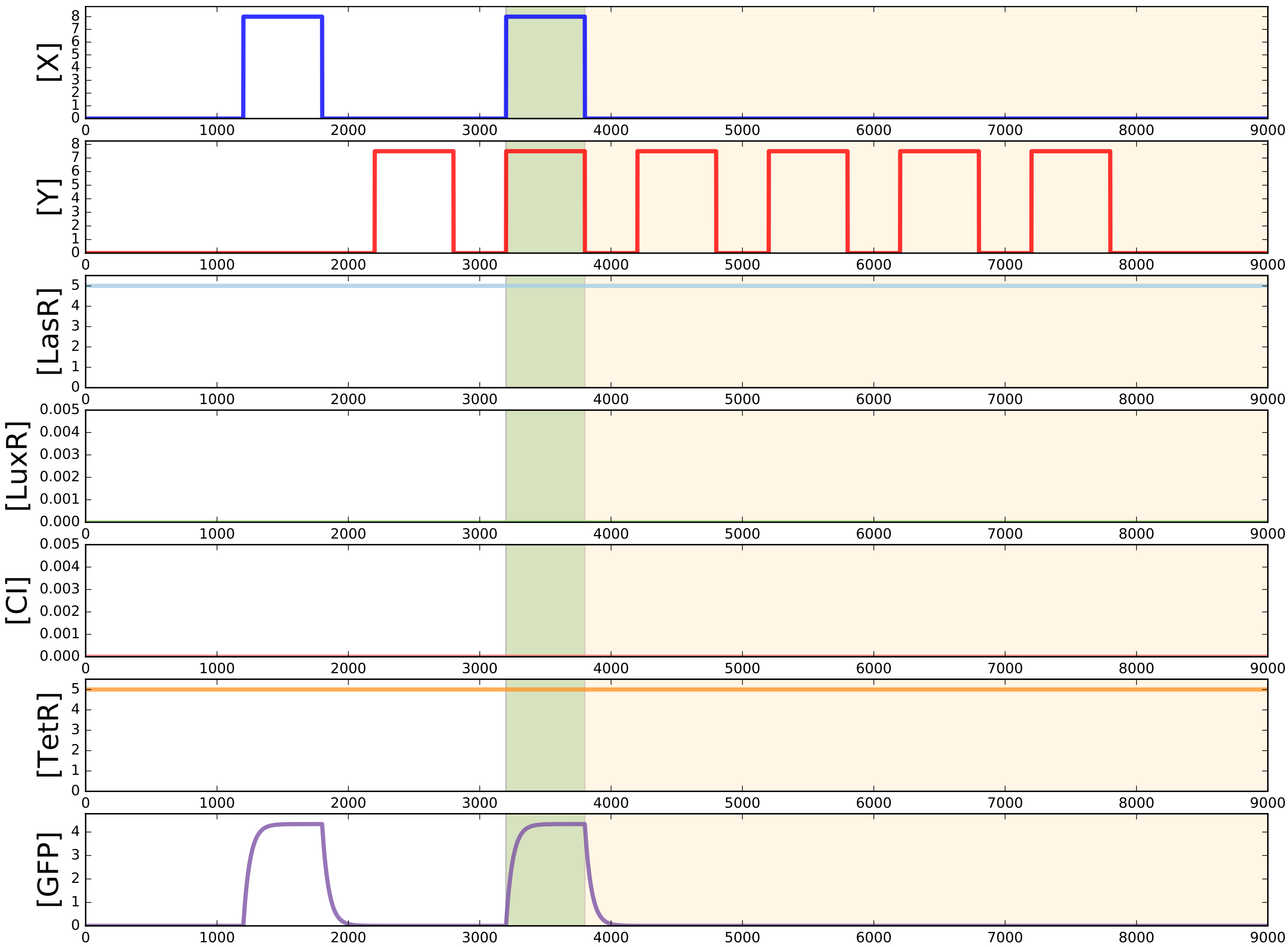

FIG. 1: Producer cell dynamics under the learning stimulation. The parameter used for this simulation are the same used for the Fig.2 in the main text.

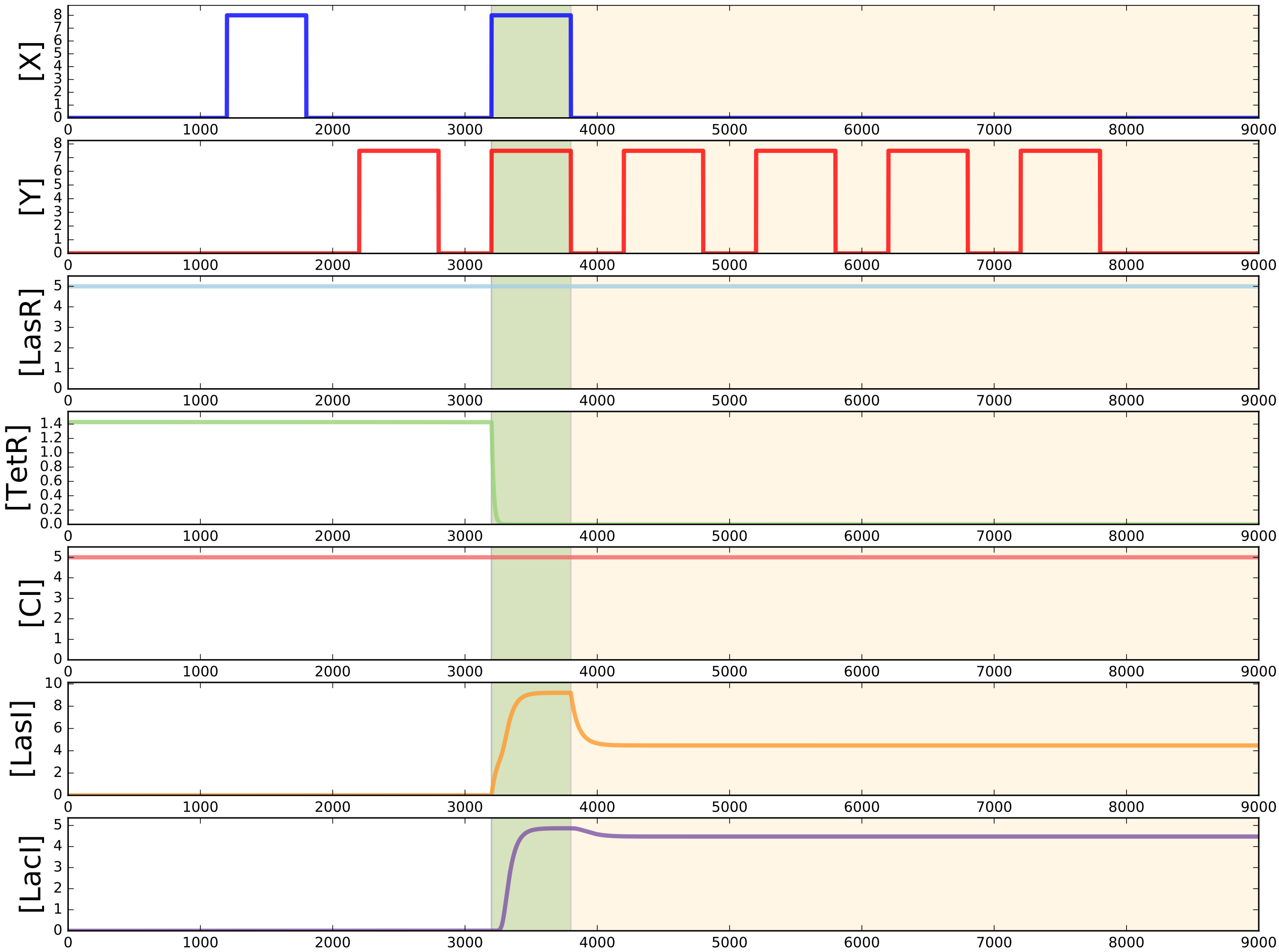

FIG. 2: Learning cell dynamics under the learning stimulation. The parameter used for this simulation are the same used for the previous figures.

2. PHASE SPACE ASSOCIATIVE LEARNING (VIA TOGGLE-SWITCH) DEPENDING ON γ_A

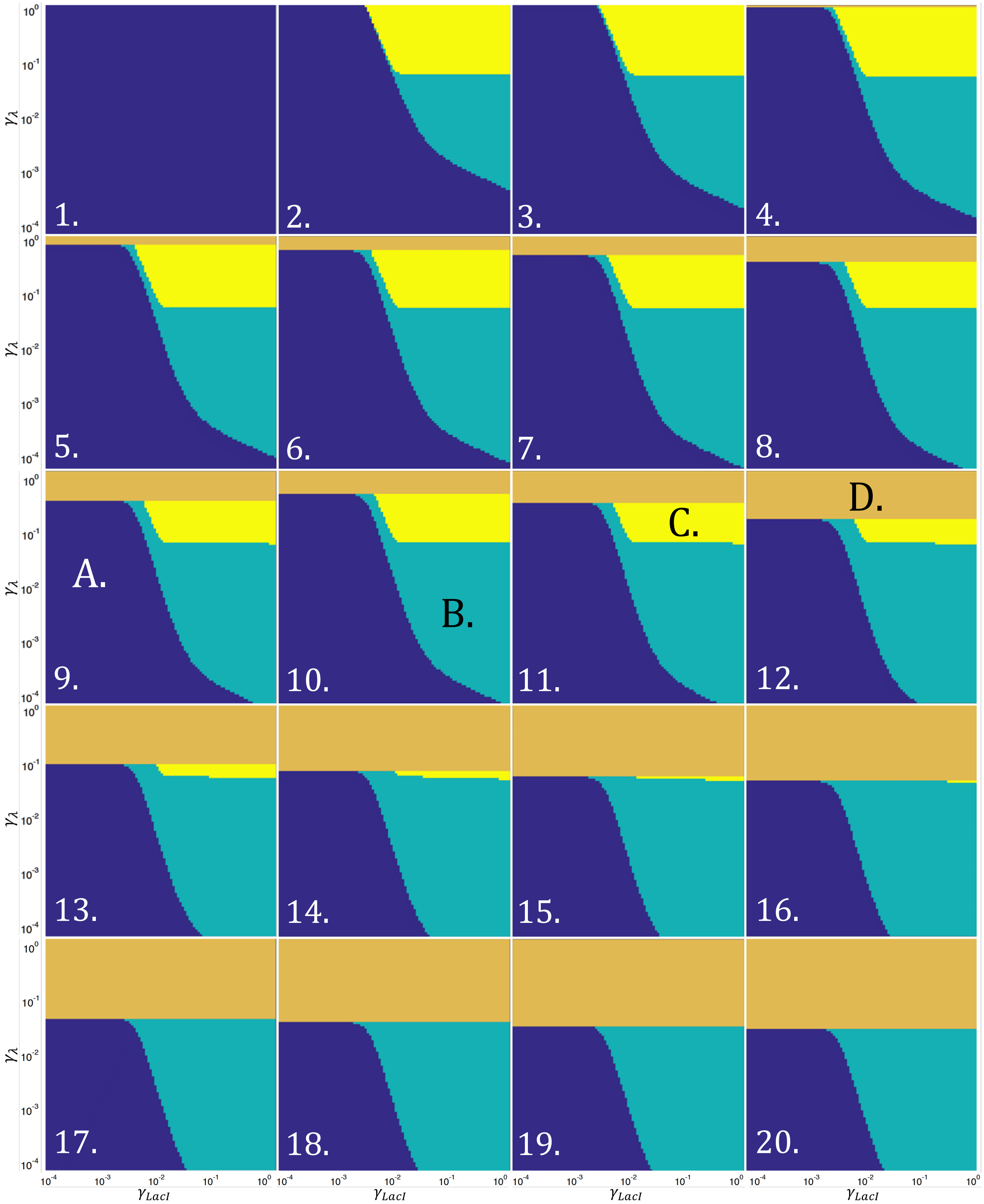

FIG. 3: Phase space depending on γ_A. From 1. to 11. the values of γ_A are from 0 to 0.1 with an increment of 0.01. The rest of phase spaces (11.-20.) the increment is 0.1, then the production rate at the phase space 20. is 1. The other parameters are the same as the previous figures; the supplementary phase spaces are done using a regular 100x100 latice.

3. WHOLE SPECIES SPACES

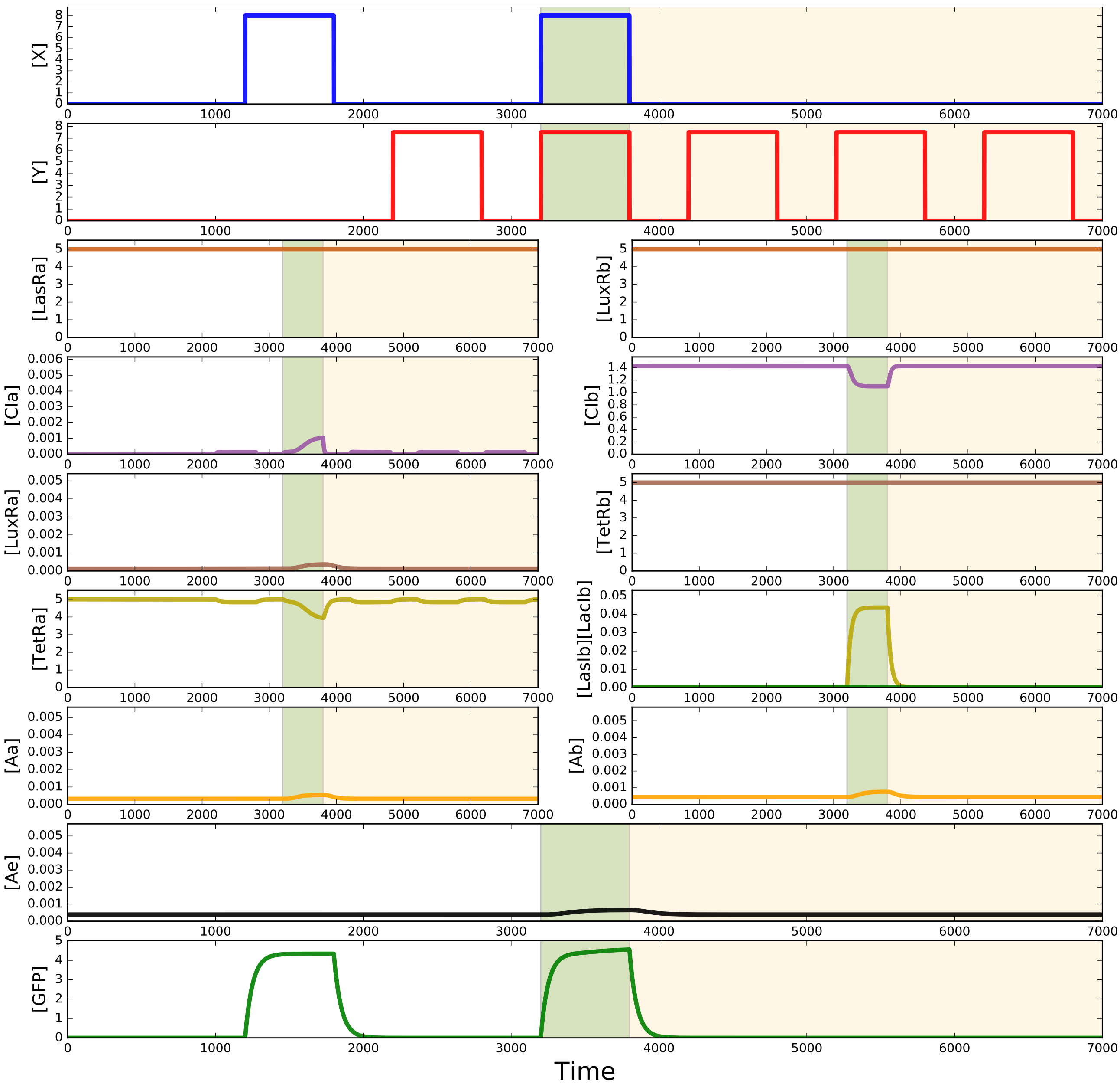

FIG. 4: No Learning. The GFP signal shows that the systems responds to the non-conditioned signal X. The parameter values are $\gamma_{LacI} = 10^{-3}$ and $\gamma_{\lambda} = 10^{-1}$; the other parameters are fixed to the same used in the previous figures.

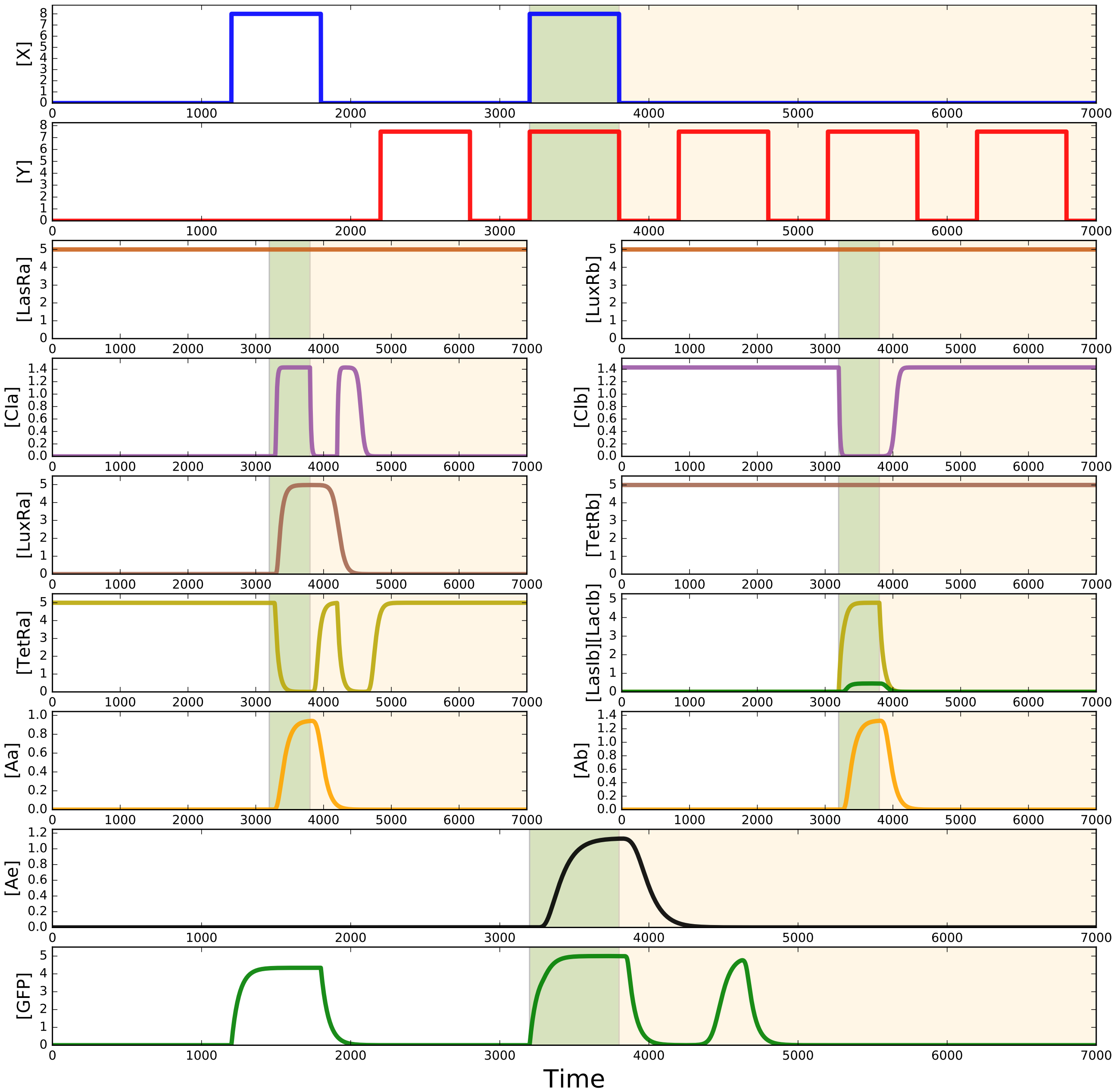

FIG. 5: Damped Learning.The GFP signal shows that the systems responds to the non-conditioned signal X and the conditioned signal Y for a period of time. The parameter values are $\gamma_{LacI} = 10^{-1}$ and $\gamma_{\lambda} = 10^{-2}$; the other parameters are fixed to the same used in the previous figures.

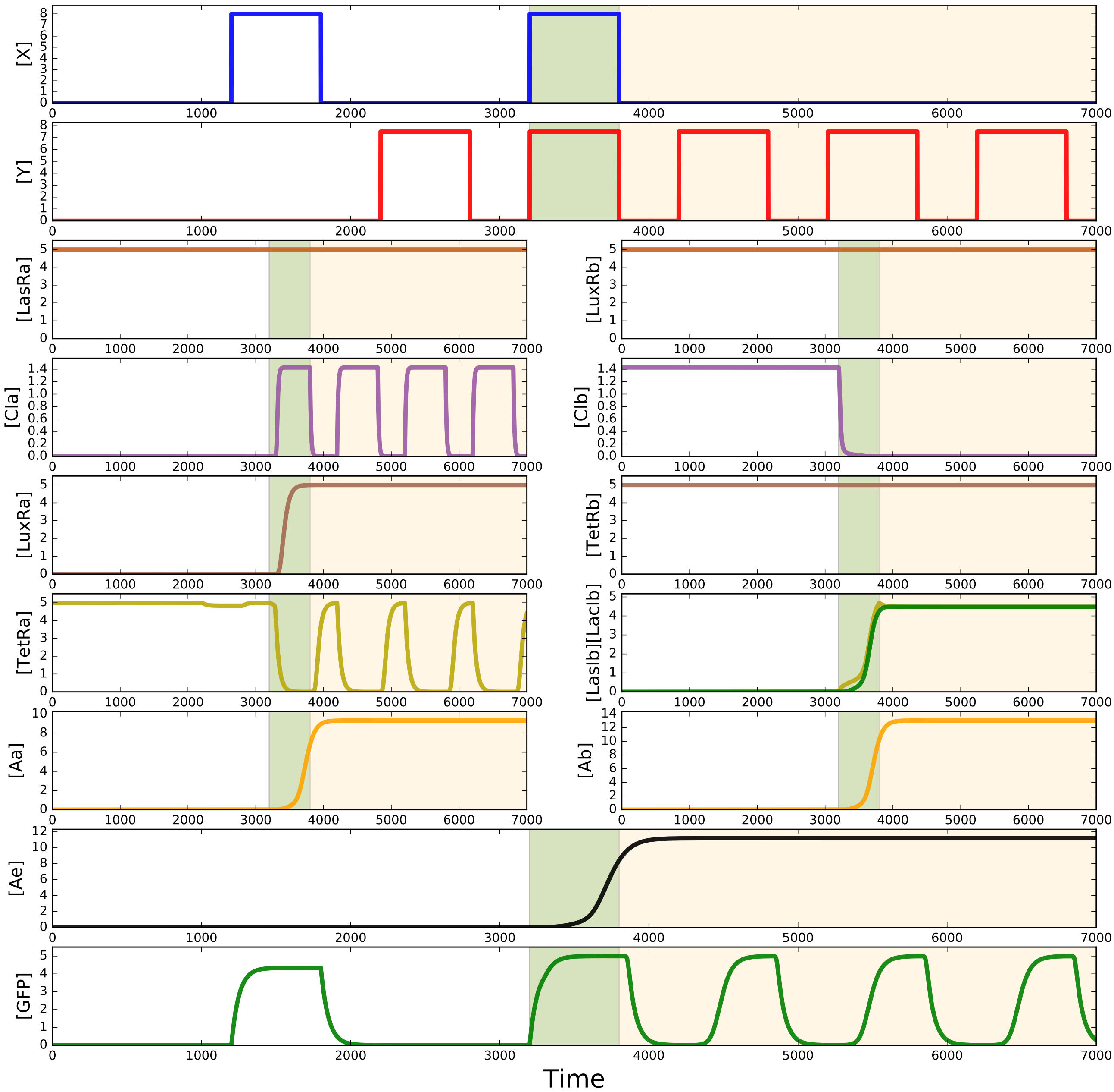

FIG. 6: Associative Learning. The output signal (GFP) shows that after a conditioning process (simultaneous stimulation with X and Y) the systems is capable to responds to both signals. The parameter values are $\gamma_{LacI} = 10^{-2}$ and $\gamma_{\lambda} = 10^{-1}$; the other parameters are fixed to the same used in the previous figures.

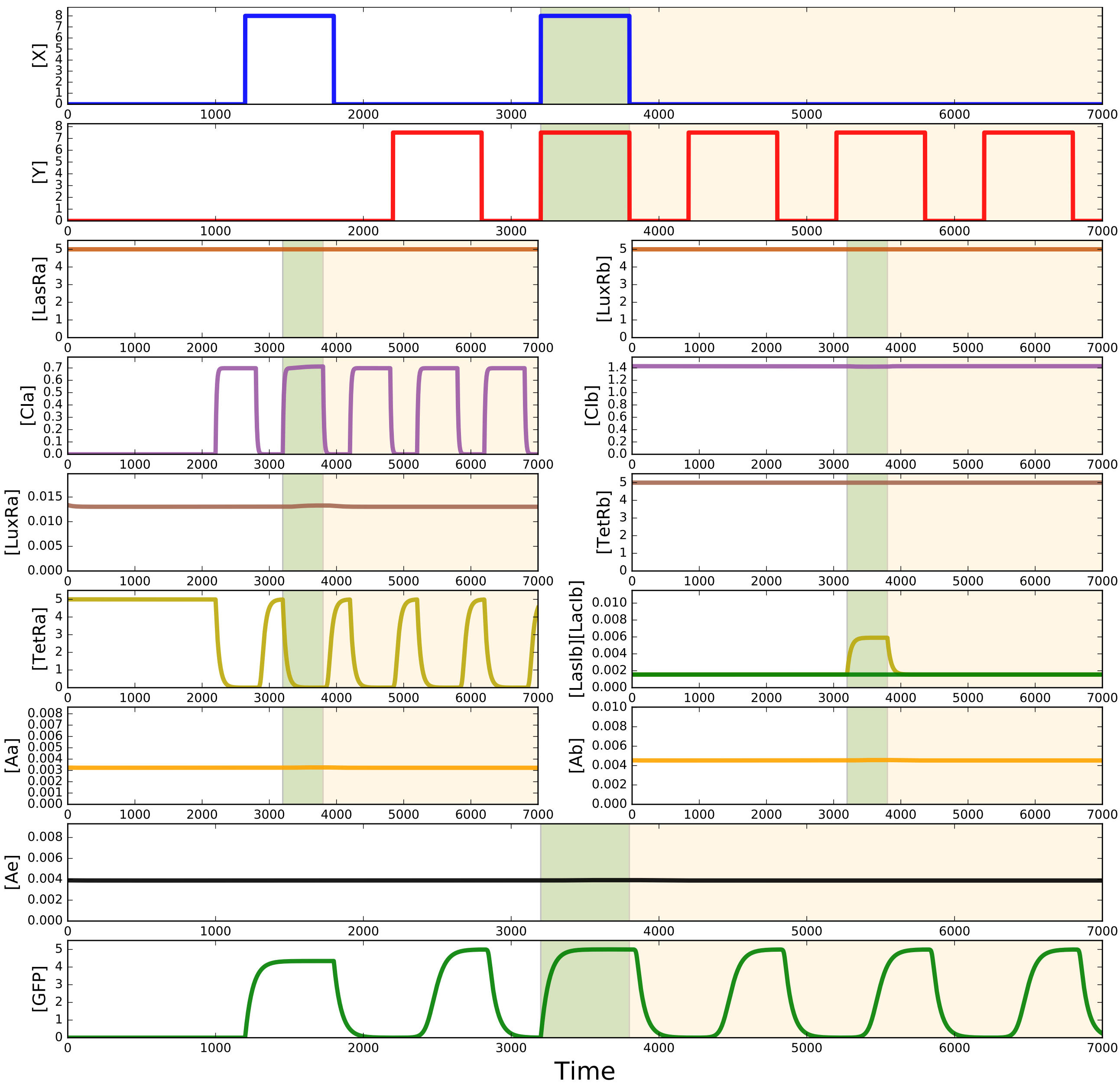

FIG. 7: Non learning responding system. The system of two cells is able to responds to both stimuli even before they are conditioned. The parameter values are $\gamma_{LacI} = 10^{-4}$ and $\gamma_{\lambda} = 10^{0}$; the other parameters are fixed to the same used in the previous figures.

4. MODEL DESCRIPTION OF ASSOCIATIVE LEARNING (POSITIVE FEEDBACK LOOP)

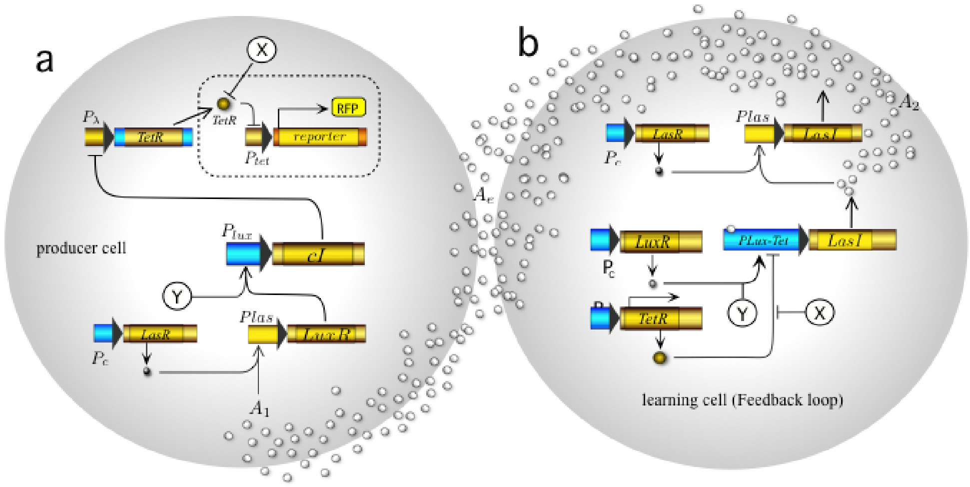

FIG. 8: Complete diagram of the Associative Learning motif using positive feedback loop.

For the design of a learning cell using a positive feedback loop we have considered the following different set of equations.

There are three genes are expressed constitutively to be receptors of the three different signals (X , Y and the inner signalling molecule A) , they are modelled by linear equations:

$$\frac{d[LuxR]}{dt} = \gamma_{LuxR} - \delta_{LuxR}[LuxR] \tag{1}$$

$$\frac{d[TetR]}{dt} = \gamma_{TetR} - \delta_{TetR}[TetR] \tag{2}$$

$$\frac{d[LasR]}{dt} = \gamma_{LasR} - \delta_{Las}[LasR] \tag{3}$$

The inducer protein $LasI$ is produced in two different constructs. First, an induced production by the simultaneous stimulation with X and Y. And secondly, the production due to the the binding of the effector molecule A and their receptor $LasR$; this construct is the positive feedback loop.

$$\frac{d[LasI]}{dt} = \gamma_\lambda\Gamma_2 + \gamma_\lambda\Gamma_3\Gamma_1 - \delta_{LasI}[LasI] \tag{4}$$

5. MODEL DESCRIPTION OF DAMPED LEARNING ALTERNATIVES

First design

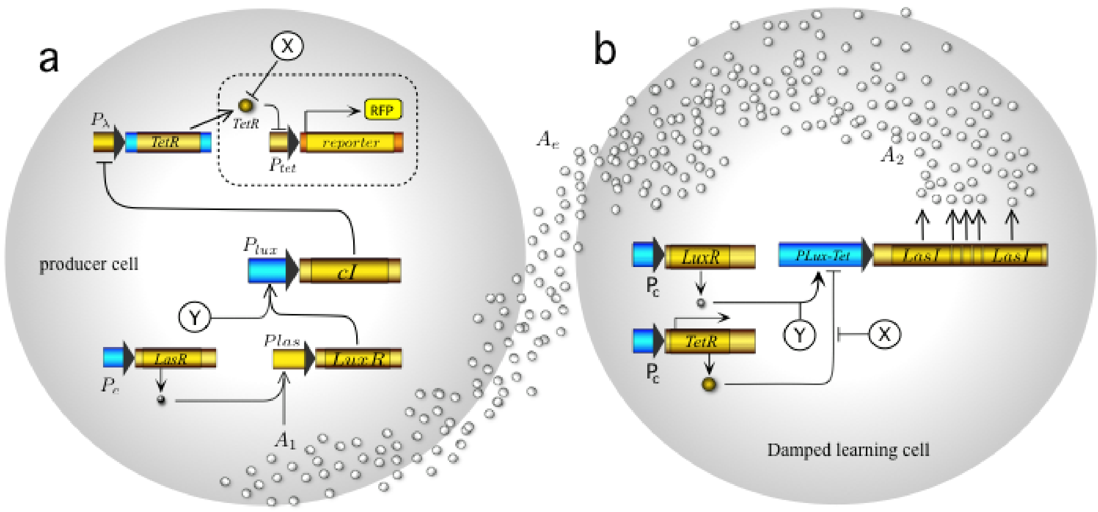

FIG. 9: Complete diagram of the Damped Learning motif.

Here two genes are expressed constitutively thus involving linear equations:

$$\frac{d[LuxR]}{dt} = \gamma_{LuxR} - \delta_{LuxR}[LuxR] \quad (5)$$

$$\frac{d[TetR]}{dt} = \gamma_{TetR} - \delta_{TetR}[TetR] \quad (6)$$

which their gene products will be the receptors of X and Y within the cell

$$\frac{d[LasI]}{dt} = \#_{LasI}\Gamma_3\Gamma_1 - \delta_{LasI}[LasI] \quad (7)$$

Second design

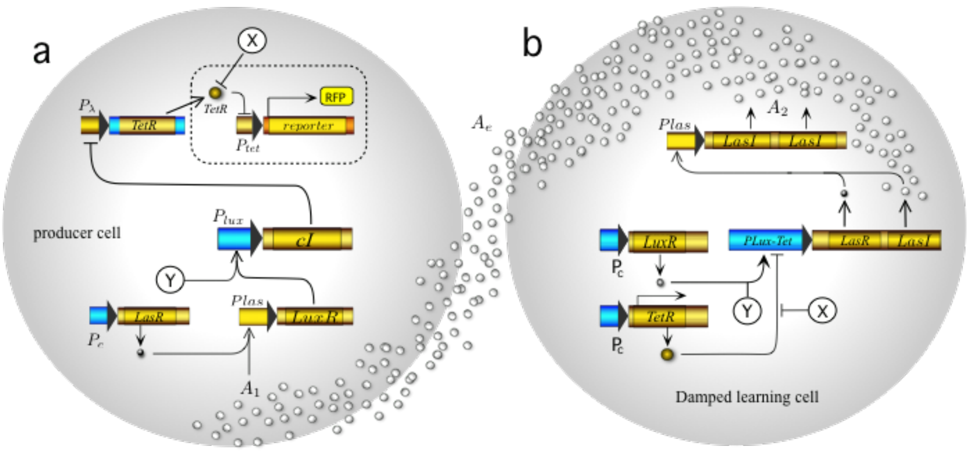

FIG. 10: Complete diagram of the Damped Learning motif.

Here two genes are expressed constitutively thus involving linear equations:

$$\frac{d[LuxR]}{dt} = \gamma_{LuxR} - \delta_{LuxR}[LuxR] \quad (8)$$

$$\frac{d[TetR]}{dt} = \gamma_{TetR} - \delta_{TetR}[TetR] \quad (9)$$

which their gene products will be the receptors of X and Y within the cell

$$\frac{d[LasR]}{dt} = \gamma_{LasR}\Gamma_3\Gamma_1 - \delta_{LasR}[LasR] \quad (10)$$

$$\frac{d[LasI]}{dt} = \#_{LasI}\Gamma_2 + \gamma_{LasI}\Gamma_3\Gamma_1 - \delta_{LasI}[LasI] \quad (11)$$