# Model specification of a two cell model

Here we describe the specifications of the two cell system represented in Figure 1A of this document.

#### The Boolean networks

The Boolean network for each cell is specified by three arrays:

 ${\bf nv}$ : The number of variables in each Boolean function. The size of this array is  ${\bf n}$ , the number of genes in the Boolean Network.

**varF**: The variables of each function. Each variable is represented by the gene id, a number between 0 and n-1. varF is a max(nv)-by-n matrix. Variables of the functions for the first node are varF(:,0), for the second node varF(:,1), ..., and for the last node varF(:,n-1). Since the number of variables may vary between different functions, only the first nv(i) elements are relevant in the i:th column of varF. Remaining "unnecessary" elements in each column are set to -1.

**F**: The functions for the random network. F has size  $2^{\text{max}(\text{nv})}$ -by-n. Truth tables of the functions for the first node are defined in F(:,0), for the second node F(:,1), ..., and for the last node F(:,n-1). Since the length of the truth tables may vary between different functions, only the first  $2^{\text{nv}(i)}$  bits are relevant in the i:th column of F. Remaining "unnecessary" bits in each column are set to -1. Let the f = F(:,i) be the function with index i in F, and assume that it is a function of three variables xi, xj, and xk (variables are defined in varF(0:2,i). Then, f(0) defines the output for the input vector (000). Correspondingly, f(1) defines the output for the input vector (001), where xi=xj=0 and xk = 1, i.e., where the third input variable is equal to one. As another example, f(5) defines the output for the input vector (101), where xi = 1, xj = 0, and xk = 1.

The file "Models/example1/example1.nv" specifies the nv arrays for cell 0 (first row) and cell 1 ( second row), the file "Models/example1/example1.varf" specifies the varF arrays for both cells ( the first 2 rows for cell 0 and the last 2 rows for cell 1), and the file "Models/example1/example1.tt" specifies the F arrays for both cells ( the first 4 rows for cell 0 and the rest for cell 0).

## The cytokine network

The cytokine network is defined by a table, see Figure 1B, in which the first column determines if the row specifies a receptor of a cytokine (R) or if the row specifies the secretion of a cytokine (S). The second column specifies the id of the cytokine, an index starting from 0. The third column specifies the cell id, the fourth column specifies the gene id, and the fifth column

specifies the activation threshold if the first column is (R) and the secretion rate if the first column is (S).

The file "Models/example1/example1\_cytonet.txt" specifies the cytokine network for the two cell model described in Figure 1.

## **Cell positions**

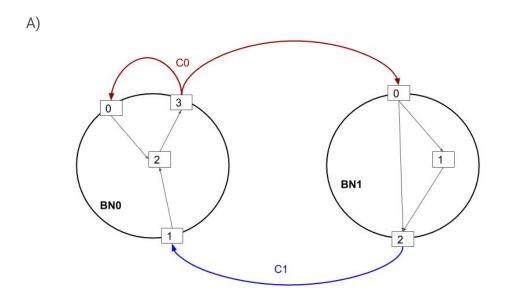
The code reads the number of cells of the system and the positions and ID for every cell from an input file. The first row of the file indicates the number of cells. The positions and cell IDs of the cells are read from the second row. The first three columns indicates the XYZ coordinates of a cell and the fourth columns indicates its cell ID.

The python script 'run\_example1.py' creates the file with cell coordinates and IDs for the two cell model described in Figure1.

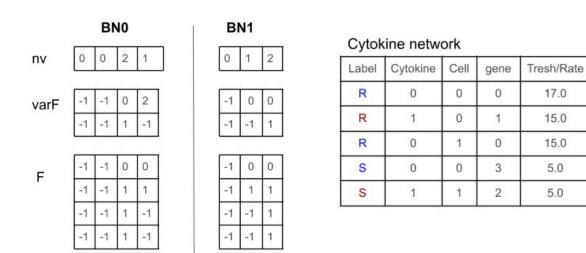
#### **Initial States**

To start simulations we need to specify the initial state (0 or 1) of each gene of each cell. The initial states are specified by a file with the number of columns equal to the maximum number of genes considering all the cell types. The number of rows should be equal to the number of cells.

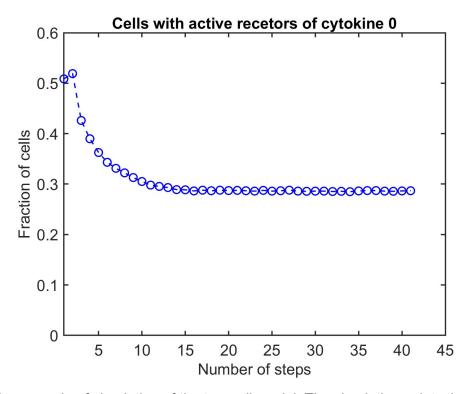
The python script 'run\_example1.py' creates the files with initial Boolean states for the two cell model described in Figure 1.



B)



**Figure 1** A) Schematic representation of a two cell systems. Each cell is endowed with a Boolean Network, BN0 and BN1. The cells interact through two cytokines, C0 and C1. B) Tables to specify the two cell systems



**Figure 2.** An example of simulation of the two cell model. The simulations plots the fraction of cells with activated receptors of cytokine 0.