A new model for the immune clonal networks

V. V. Gafiychuk* and A.K. Prykarpatsky†

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Abstract

This paper deals with a new model for clonal network dynamics. We describe in detail this model and derive special equations governing immune system dynamics based on the general gradient type principles that can be inherent to a wide class of real living objects. A special clonal network is modeled by two symmetric projector matrix variables simultaneously taking into account both asymmetry of the interaction to each other and adaptation states that can be realized owing to possible idiotypic clonal suppresions. We perform computer simulations of the model dynamics for some simple cases of relatively low dimension, paying special attention to the dynamics of amounts of activated receptor strings within clonal network.

keywords: clonal dynamics, immune system, mathematical model, gradient dynamical system, Lyapunov function, computer simulation, complex system.

1 Introduction

The dynamics of clonal network is a very important problem for understanding immune systems dynamics and starting from the first mathematical model of Jerne [18] a lot of mathematical models are used for modeling it (See, for example [24, 7, 19, 25, 4, 21]). It is very well known that immune system contains many types of B-cells which can activate each other at certain conditions. If the receptors of such B-cells match each other the cells become antibody cells and they effectively recognize antigens [24, 25, 4, 21]. The construction of the cell gene model allows one to understand how the same network can support different independent state of the immune system. Among these states we can distinguish states which are quite different in their functional activity, for example a virgin state when the clone state is not activated, the immune state when

*Institute of computer modeling, Krakow University of Technology, 24 Warszawska Street, 31155, Krakow, Poland; Institute of Applied Problems of Mechanics and Mathematics NASU, Lviv, Ukraine, 79053.

†Dept. of Applied Mathematics at the AGH University of Science and Technology, 30 Mickiewicz Al. Bl. A4, 30059 Krakow, Poland; Institute of Applied Problems of Mechanics and Mathematics NASU, Lviv, Ukraine, 79053.

a clone proliferates antibody cells and finally - the inhibited state when proliferation terminates. Which state is reached depends on the local topology of the network and conditions of gene presentation With the additional assumption that the parameters of the model change between early and late states one can understand how self-nonself interaction is accomplished by the clonal network. In this case several original approaches has been proposed in order to explain characteristic features of evolution of B-cell repertoire [22, 20] and evolution of specificity in humoral immunity based on idiotypic network [13].

Dynamics of this clonal type network with symmetric interactions probably can converge [3] to steady or oscillatory state under very general assumptions [1]. But in reality interactions between clones are not confined to steady states (attractors) but also include other almost periodic and aperiodic behaviors. The interaction between an excitatory and inhibitory clone is clearly asymmetric. Assume that a self basic gene is seen by its own clone. Recall [17] that adaptation can be achieved by the suppression of this idiotypic clone by the corresponding anti-idiotypic clone. Once the adaptation state is achieved, secondary presentation of the leading gene does not give rise to any network response, because the gene only increases the suppression on its clone. It would be interesting to observe if some basic modifications to the governing network model equations could be made that allow really memory retention [11, 12]. If it is not the case, then not being able to retain memory of former inhibitory gene encounters may not be failing of the model under regard but rather a reflection of the intrinsic properties of clonal network.

The model is composed [24, 26, 5, 23, 16, 27, 28] of a varying number of cell clones of different specificities that form a clonal network. Each clone is characterized by its specific inhibitory and excitatory receptors, which are specified in the model by bit strings and clonal receptor string $x_\alpha \in \mathbb{R}^n, \alpha \in \mathcal{N}_x$ and $y_\beta \in \mathbb{R}^n$, $\beta \in \mathcal{N}_y$, normalized by the conditions $\|x_\alpha\| = 1$ and $\|y_\beta\| = 1$ allowing for some components to bring either positive or negative signs. Thereby this makes it possible to achieve suitable adaptation state through the related suppression of idiotypic clone by the corresponding anti-idiotypic clone, whose modeling within our clonal network is realized in the framework of the postulated self-similarity of gene action and asymmetry of clone interaction. Two clones can interact via soluble inhibitory genes whenever their receptor shapes, i.e. bit strings are complementary. Cells that become activated proliferate and differentiate into inhibitory secreting cells. This process takes some time during which another free inhibitory cells form dynamic complexes not taking often real role within excitatory-inhibition network dynamics.

The existence of invariant localized dynamic patterns says that our idiotypic clonal network possesses certain self-structured properties. Asymmetric interactions within the network determinate network's working size and connectivity and determine the total inhibitory cells level. Concerning the connectivity within the network one can conclude that the network in equilibrium selects for growth and retaining within the network the clones with low connectivity. Within this framework low connectivity is not an intrinsic property of any particular inhibitory cell but rather is determined by the random structure of a

clone's receptor and the shapes of the receptors on the other clones presented in the system.

The incorporation of this meta-dynamics in this excitatory-inhibitory model one can consider as an attempt to account for the rapid enough turn over of clones in the clonal network. Such processes were also studied in [16, 27, 8, 2, 9] within a cellular automation approach. There was found that networks of automata can be considered as dynamical systems being the discrete equivalent of differential systems. They have been recently widely used in clonal nets and cellular automata to model complex systems such as brain. One of the main advantages of these networks for a biologist involved in modeling is that the construction of a model requires a minimal knowledge about the numerical values of the parameters defining a system. The differential equation systems describing require biological data on cell lifetimes like thresholds for activation, affinity constraints of the network dynamics. Most automata models do not require these data, since the basic assumption is that sell populations need only be described by a set of some discrete values, often 0 and 1, where 0 means that a populations absent, while 1 means that it is presented at a high enough level. The corresponding interactions among populations are represented by logical functions, i.e. Boolean set function, which most often are equivalent to threshold automata like physical spin systems [16, 27, 8, 2]. Such a modeling can be applied to a wide class of complicated neural networks taking into account different states of development of the corresponding cells and also to system evolution differential equations discussed below. These aspects of studying our excitatory-inhibitory clonal type network are planned to be discussed in more detail in another place. In this paper we will use in part an approach devised in for [14, 15] describing evolution of the introduced clonal network.

2 Clonal network model description

A network under consideration models a clonal dynamics exhibiting excitatory-inhibitory properties. It consists of interacting cell clones generated by inhibitory and excitatory genes within a fixed medium. The latter will be called a configuration phase space, depending strongly on the nature of interaction between clones. An inhibitory clone population within the network can be effectively encoded, in general, by a real $(n \times n)-$ asymmetric projector matrix of the canonical [10] form $X := \sum\limits_{\alpha \in \mathcal{N}_x}^{n(x)} x_\alpha \otimes \hat{x}_\alpha \in End\mathbb{R}^n$, where biorthogonal to each other vectors $x_\alpha, \hat{x}_\alpha \in \mathbb{R}^n$, $\alpha \in \mathcal{N}_x \subset \overline{1,n}$, are the corresponding reciprocity receptor strings amplitudes responsible for an inhibitory clonal topology within the network and the number $card\mathcal{N}_x = n(x) \in \mathbb{Z}_+$ means exactly the amount of activated receptors belonging to the inhibitory clone. The inhibitory clonal self-similarity is realized now by means of the fundamental projector property $X \cdot X = X$ for all whiles of time.

Similarly, an excitatory population can be encoded, in general, by real

$(m\times m)$ -asymmetric projector matrix of the canonical form $Y := \sum\limits_{\beta\in\mathcal{N}_y}^{n(y)} y_\beta \otimes \hat{y}_\beta \in End\mathbb{R}^m$, where biorthogonal to each other excitatory vectors $y_\beta, \hat{y}_\beta \in \mathbb{R}^m$, $\beta \in \mathcal{N}_y \subset \overline{1,m}$, are the corresponding reciprocity receptor strings amplitudes responsible for an excitatory clonal receptor topology and $card\mathcal{N}_y = n(y) \in \mathbb{Z}_+$ means the amount of activated excitatory receptors during the network dynamics. The excitatory clonal self-similarity is realized here also by means of the fundamental projector property $Y \cdot Y = Y$ for all whiles of time. In general, the integer numbers $n(x), n(y) \in \mathbb{Z}_+$ can change during the network dynamics because of the possible full suppression of some activated clone receptor strings. Concerning the interaction between the clonal populations, it is described by means of a real $(m \times n)$ -matrix $Z := \sum\limits_{\alpha\in\mathcal{N}_x}^{n(x)} \sum\limits_{\beta\in\mathcal{N}_y}^{n(y)} z_{\beta\alpha} y_\beta \otimes \hat{x}_\alpha \in Hom(\mathbb{R}^n;\mathbb{R}^m)$ with parameters $z_{\beta\alpha} \in \mathbb{R}$, $\alpha \in \mathcal{N}_x \subset \overline{1,n}$, $\beta \in \mathcal{N}_y \subset \overline{1,m}$, responsible for the strengths of interaction between receptors strings of two clonal populations. The adaptation of some inhibitory or excitatory during interaction clones is modeled within our clonal network by means of a possible time dependence of corresponding strength parameters $z_{\beta\alpha} \in \mathbb{R}$, $\alpha \in \mathcal{N}_x \subset \overline{1,n}$, $\beta \in \mathcal{N}_y \subset \overline{1,m}$, that the matrix Z necessarily satisfies the next important self-similar clonal interaction properties $ZX = Z = YZ$ for all whiles of time.

3 Clonal network topology and dynamics

It is natural to endow our configuration phase space $M_{(x,y,z)} \subset (End\mathbb{R}^n \times End\mathbb{R}^m) \times Hom(\mathbb{R}^n;\mathbb{R}^m)$ with a reasonable Riemannian metrics by means of the following scalar product on its tangent space $T(M)$:

$$\left\langle (X,Y,Z),(\widetilde{X},\widetilde{Y},\widetilde{Z})\right\rangle := tr(X^T\widetilde{X}) + tr(Y^T\widetilde{Y}) + tr(Z^T\widetilde{Z}) \tag{1}$$

where $X,\widetilde{X} \in T(End\mathbb{R}^n), Y,\widetilde{Y} \in T(End\mathbb{R}^m)$ and $Z,\tilde{Z} \in T(Hom(\mathbb{R}^n;\mathbb{R}^m))$ are arbitrary elements of the corresponding tangent spaces. Concerning the metrics (1) one can construct a gradient vector field on the projector field manifold $M_{(x,y,z)}$ generated by the Lyapunov interaction function $\Phi : M \to \mathbb{R}$ whose variation is

$$\delta\Phi(X,Y,Z) := tr(D_h^T\delta Z) + tr(D_f^T\delta X) + tr(D_g^T\delta Y) \tag{2}$$

for some specified matrices $D_f \in T(End\mathbb{R}^n)$, $D_g \in T(End\mathbb{R}^m)$ and $D_h \in T(Hom(\mathbb{R}^n;\mathbb{R}^m))$, being responsible for the asymmetry of the interaction between clonal populations. Except the Lyapunov function variation (2) it is necessary to involve into the picture the following natural clonal phase constraints:

$$\begin{aligned} tr(A^T(X^2 - X)) &= 0,\ tr(B^\intercal(Y^2 - Y)) = 0, \\ tr((ZX - Z)Q^\intercal) &= 0,\ \ tr((YZ - Z),R^T) = 0, \end{aligned} \tag{3}$$

holding for any $A \in End\mathbb{R}^n, B \in End\mathbb{R}^m$ and $Q, R \in Hom(\mathbb{R}^n; \mathbb{R}^m)$. Constraints (3) can be still augmented in many special cases by the symmetry conditions

$$tr((X^\intercal - X)P^\intercal) = 0, \quad tr((Y^\intercal - Y)S^\intercal) = 0, \tag{4}$$

holding also for arbitrary matrices $P \in End\mathbb{R}^n$ and $S \in End\mathbb{R}^m$.

Below we will consider only this strongly symmetric case of our clonal network. Concerning the constraint conditions involved above the corresponding gradient vector field generated by the Lyapunov function variation (2) is given as

$$\begin{aligned} dX/dt &= [[D_f, X], X] + \\ &+(Z^\intercal Z + 2I)^{-1}(Z^\intercal D_h - Z^\intercal Z D_f)(1 - X) + \\ &+(1 - X)(D_h^\intercal Z - D_f Z^\intercal Z)(Z^\intercal Z + 2I)^{-1}, \\ dY/dt &= [[D_g, Y], Y] + \\ &+(1 - Y)(D_h Z^\intercal - D_g Z Z^\intercal)(Z Z^\intercal + 2I)^{-1} + \\ &+(2I + Z Z^\intercal)^{-1}(Z D_h^\intercal - Z Z^\intercal D_g)(1 - Y), \\ dZ/dt &= -D_h X - Z D_f X + \\ &+2(Y - 1)(D_h X - D_g Z)(Z^T Z + 2I)^{-1} + \\ &+Z(Z^T Z + 2I)^{-1}(Z^\intercal D_h - Z^\intercal Z D_f)(1 - X) \end{aligned} \tag{5}$$

with the canonical [10] representations $X := \sum\limits_{\alpha \in \mathcal{N}_x}^{n(x)} x_\alpha \otimes x_\alpha \in End\mathbb{R}^n$, $Y := \sum\limits_{\beta \in \mathcal{N}_y}^{n(y)} y_\beta \otimes y_\beta \in End\mathbb{R}^n$, $\langle x_\alpha, x_{\alpha'} \rangle = \delta_{\alpha\alpha'}$, $\alpha, \alpha' \in \mathcal{N}_x \subset \overline{1, n}$, $\langle y_\beta, y_{\beta'} \rangle = \delta_{\beta\beta'}$, $\beta, \beta' \in \mathcal{N}_y \subset \overline{1, m}$. Here we put also $D_f = D_f^\intercal$, $D_g = D_g^\intercal$ and took the matrix $D_h \in T(End(\mathbb{R}^n; \mathbb{R}^m))$ arbitrary.

The gradient vector field (5) can be more specified if to take into account the following Lyapunov function special case taking into account the corresponding self-symmetry clonal declinations:

$$\Phi^{(1)} = tr(\alpha_h(Z - X\beta_f Z^\intercal \beta_g^\intercal Y) + tr(Z^\intercal - Y\beta_g Z \beta_f^\intercal X)\alpha_h^\intercal), \tag{6}$$

where $(X, Y, Z) \in M_{(x,y,z)}$ and $\beta_f \in End\mathbb{R}^n$ and $\beta_g \in End\mathbb{R}^m$ are some constant matrices which are close to unity matrices with respect to the corresponding norms in $End\mathbb{R}^n$ and $End\mathbb{R}^m$. Then owing to the definition (2), one finds that

$$\begin{aligned} D_h^{(1)} &= 2(\alpha_h - \beta_g^\intercal Y \alpha_h X), \\ D_f^{(1)} &= -(\beta_f Z^\intercal \beta_g^\intercal Y \alpha_h + \alpha_h^\intercal Y \beta Z \beta_f^\intercal), \\ D_g^{(1)} &= -(\alpha_h X \beta_f Z^\intercal \beta_g^\intercal + \beta_g Z \beta_f^\intercal Z \alpha_h^\intercal), \end{aligned} \tag{7}$$

Similarly one can take the following Lyapunov type function

$$\begin{aligned} \Phi^{(2)} &= tr(\alpha_{h,f}(Z^\intercal - X\beta_f Z^\intercal)) + tr(\alpha_{h,g}(Z^\intercal - Z^\intercal \beta_g Y)) + \\ &tr((Z - Z\beta_f^\intercal X)\alpha_{h,f}^\intercal) + tr((Z - Y\beta_g^\intercal Z)\alpha_{h,g}^\intercal), \end{aligned} \tag{8}$$

where $(X, Y, Z) \in M_{(x,y,z)}$, $\beta_f \in End\mathbb{R}^n$ and $\beta_g \in End\mathbb{R}^m$ are some constant matrices which are close to unity matrices with respect to the corresponding norms in $End\mathbb{R}^n$ and $End\mathbb{R}^m$. Then owing to the definition (2), one finds easily that

$$\begin{aligned} D_h^{(2)} &= 2\alpha_{h,f}(I - X\beta_f) + 2(I - \beta_g Y)\alpha_{h,g}, \\ D_f^{(2)} &= -(\beta_f Z^{\intercal}\alpha_{h,f} + \alpha_{h,f}^{\intercal} Z\beta_f^{\intercal}), \\ D_g^{(2)} &= -(\beta_g^{\intercal} Z\alpha_{h,g}^{\intercal} + \alpha_{h,g} Z^{\intercal}\beta_g). \end{aligned} \tag{9}$$

It has to be mentioned here that the Lyapunov function (6) models in general an asymmetric case of the mutual interaction between inhibitory and excitatory clone populations, realizing a really observed pattern formation structure, when the whole system is both under an external medication and intrinsically activated immune state [6].

The special analysis still must be done concerning the possible similarities between receptor sets of inhibitory and excitatory genes. This means that some mutual relationship between projector clone operators can be realized. For instance, their complete weak orthogonality can be realized and the following additional constraint

$$tr(Y\xi X\eta^T) = 0 \tag{10}$$

for all $(X, Y, Z) \in M_{(x,y,z)}$ and some constant matrices $\xi, \eta \in Hom(\mathbb{R}^n; \mathbb{R}^m)$ can hold. The condition (10) gives rise to a little complicated gradient field like (5) in part reflecting the mentioned above pattern isolating property of our clonal populations.

It can be also interesting to analyze the dynamical system (8) in the case when either projector matrices $X \in End\mathbb{R}^n$ or $Y \in End\mathbb{R}^m$ or both ones model clonal populations with the fixed number of the corresponding receptor strings activated during the interaction between them be realized that can happen when the clonal network is activated artificially by means of some external medication. This means that integers $trX = n(x) \in \mathbb{Z}_+$ or $trY = n(y) \in \mathbb{Z}_+$ persist to be fixed during the system evolution. Then these integers must be conserved quantities for all $t \in \mathbb{R}$ involving the additional scalar constraints. The latter gives rise to a little modified gradient dynamical system like (5) which we do not write down here, being obtained the same way as before.

4 Spectral analysis

Consider now two respectively biorthogonal systems of vectors $x_\alpha \in \mathbb{R}^n$, $\alpha \in \mathcal{N}_x \subset \overline{1,n}$, and $y_\beta \in \mathbb{R}^m, \beta \in \mathcal{N}_y \subset \overline{1,m}$, being eigenvectors of the symmetric projector matrices $X = X^{\intercal} \in End\mathbb{R}^n$ and $Y = Y^{\intercal} \in End\mathbb{R}^m$, respectively, satisfying [10] the following conditions:

$$Xx_\alpha = x_\alpha\,, \quad Yy_\beta = y_\beta \tag{11}$$

for all $\alpha \in \mathcal{N}_x \subset \overline{1,n}$ and $\beta \in \mathcal{N}_y \subset \overline{1,m}$. By differentiating the equalities (11) with respect to the time, one gets that

$$dX/dt\ x_\alpha + Xdx_\alpha/dt = dx_\alpha/dt, \quad dY/dt\ y_\beta + Ydy_\beta/dt = dy_\beta/dt \tag{12}$$

for all $\alpha \in \mathcal{N}_x \subset \overline{1,n}$ and $\beta \in \mathcal{N}_y \subset \overline{1,m}$. Making use of the equations (5) and (11), one has that

$$\begin{aligned} [(I-X)(D_fX - XD_f) + K_f(I-X) + (I-X)K_f]\, x_\alpha &= (I-X)dx_\alpha/dt, \\ [(I-Y)(D_gY - YD_g) + K_g(I-Y) + (I-Y)K_g] &= (I-Y)dy_\beta/dt, \end{aligned}$$

where, by definition, matrices $K_f \in End\mathbb{R}^n$, $K_g \in End\mathbb{R}^m$ and denote the corresponding out commutative parts of first two equations in (5). As a result of simple computations one gets that

$$\begin{aligned} (I-X)(D_fX - XD_f)x_\alpha + (I-X)K_fx_\alpha &= (I-X)dx_\alpha/dt, \\ (I-Y)(D_gY - YD_g)y_\beta + (I-Y)K_gy_\beta &= (I-Y)dy_\beta/dt. \end{aligned} \tag{13}$$

From (13) one finds easily that

$$\begin{aligned} dx_\alpha/dt &= (D_fX - XD_f)x_\alpha + (I-X)K_fx_\alpha + Xz_\alpha^{(f)}, \\ dy_\beta/dt &= (D_gY - YD_g)y_\beta + (I-Y)K_gy_\beta + Yz_\beta^{(g)} \end{aligned} \tag{14}$$

for some vectors $z_\alpha^{(f)} \in \mathbb{R}^n$ and $z_\beta^{(g)} \in \mathbb{R}^m$ for all $\alpha \in \mathcal{N}_x \subset \overline{1,n}$ and $\beta \in \mathcal{N}_y \subset \overline{1,m}$. Since, in general, $tr(dX/dt) \neq 0$ and $tr(dY/dt) \neq 0$, we deduce that the integers $rankX$ and $rankY$ are changing in time. On the other hand, since $trX = n(x) \in \mathbb{Z}_+$ and $trY = n(y) \in \mathbb{Z}_+$ are integers, we see that our the dynamical system possesses very interesting properties related with jumping of the integers $n(x)$ and $n(y) \in \mathbb{Z}_+$ at some fixed whiles of time. This phenomenon can be interpreted naturally as a result of activation (dis-activation) of available receptor strings characterizing our interacting clonal populations during the interaction process. Returning back to equations (14) one can observe that vectors $z_\alpha^{(f)} \in \mathbb{R}^n$ and $z_\beta^{(g)} \in \mathbb{R}^m$ must satisfy the conditions

$$< z_\alpha^{(f)}, x_{\alpha'} >= 0, \quad < z_\beta^{(g)}, y_{\beta'} >= 0, \tag{15}$$

$$\begin{aligned} &< D_fx_\alpha, x_{\alpha''} > + < K_fx_\alpha, x_{\alpha''} >= 0, \\ &< D_gy_\beta, y_{\beta''} > + < K_gy_\beta, y_{\beta''} >= 0 \end{aligned} \tag{16}$$

for $\alpha, \alpha' \in \mathcal{N}_x \subset \overline{1,n}$, $\alpha'' \notin \mathcal{N}_x \subset \overline{1,n}$, and for $\beta, \beta' \in \mathcal{N}_y \subset \overline{1,m}$, $\beta'' \notin \mathcal{N}_y \subset \overline{1,m}$. Relationships (15) can be used as some criterion for the corresponding ranks of the projector matrices $X \in End\mathbb{R}^m$ and $Y \in End\mathbb{R}^m$, evolving with respect to the dynamical system (5), to become jumped.

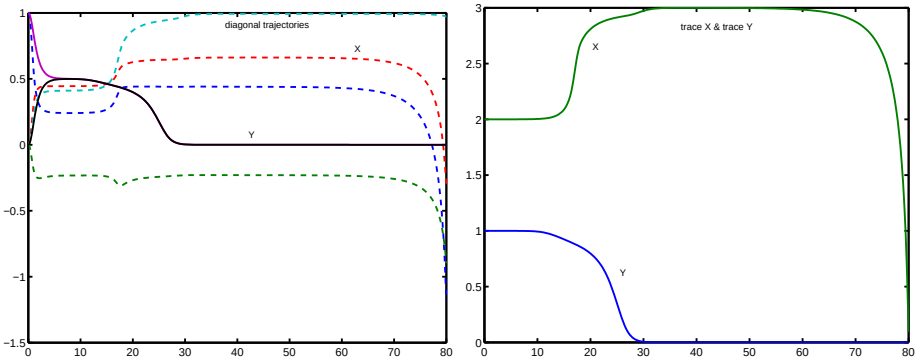
5 Clonal network simulation

So far introduced mathematical clonal network model has been written as a formal system of matrix nonlinear differential equations. In order to check the characteristic features of this system we have performed computer simulations of the model for several values of $n, m \in \mathbb{Z}_+$ and as well as for different initial conditions and forms of the corresponding constant matrices entering the system. The model is composed in general of $n(n+1)/2 + m(m+1)/2 + nm \in \mathbb{Z}_+$ scalar differential equations, i.e. of the inhibitor share equations, excitor share equations and equations describing interaction between these shares. The integration of this system requires simultaneous integrations of these scalar differential equations, each of which is a first order ODE. Let us now illustrate the dynamic behavior of our system by computer simulation at some simple starting data. We rewrite down governing equations (5) in a new equivalent form which was used for computer simulation:

$$\begin{aligned}
dX/dt &= [[D_f, X], X] + \\
&+X(XZ^\intercal YZ + 2I)^{-1}X(Z^\intercal YD_h - Z^\intercal YZXD_f)(I - X) + \\
&+(I - X)(D_h^\intercal YZ - D_f XZ^\intercal YZ)X(XZ^\intercal YZ + 2I)^{-1}X, \\
dY/dt &= [[D_g, Y], Y] + \\
&+(I - Y)(D_h XZ^\intercal - D_g YZXZ^\intercal)Y(YZXZ^\intercal + 2I)^{-1}Y + \\
&Y(2I + YZXZ^\intercal)^{-1}Y(ZD_h^\intercal - ZXZ^\intercal YD_g)(I - Y), \\
dZ/dt &= -D_h X - YZXD_f X + \\
&2(Y - I)(D_h X - D_g YZ)X(XZ^T YZ + 2I)^{-1}X + \\
&+YZX(XZ^T YZ + 2)^{-1}X(Z^\intercal YD_h - Z^\intercal YZXD_f)(I - X).
\end{aligned} \tag{17}$$

Here when writing down the system (17) we took into account constraints (3) in order to get matrix paths always lying on the corresponding projector parts of the manifold M. We used Matlab software to perform our simulation of equations (17). Despite the complex structure of equations describing our immune clonal network, its dynamical behavior is fairly interesting and good modeling some real ones.

In Fig. 1 we plotted the outcome of numerical simulations for the case $\dim X = 4$, $\dim Y = 2$. The plots in Fig. 1 show that the simulations recover perfectly the clonal network behavior predicted by both qualitative and some analytic considerations. For simplicity, we first consider the matrix D_h being zero. Fig. 1 displays a dynamics of inhibitory network X and excitatory Y at the conditions and parameters indicated in the capture of the figure. The behavior of the diagonal elements (receptors mapping antigen concentration) of the of the excitor are displayed by solid line and inhibitory receptors are displayed by dashed line. The displayed dynamics has a simple physical meaning. The receptor of activator network responsible for antigen state is getting depressed (equal to zero) due to activation of inhibitory one (Fig. 1 b). At certain value of time the state of the inhibitory network is tending to zero also.



a b

Figure 1: Behavior of the diagonal elements of matrix X - dashed line, Y- solid line a), traces of the matrices X and Y - b). Here $D_g = \begin{pmatrix} -1 & 0.5 \\ 0.5 & -1 \end{pmatrix}$, $D_f = \begin{pmatrix} 0.5 & -0.15 & 0.5 & 0.4 \\ -0.15 & 1 & 0.3 & 0.1 \\ 0.5 & 0.3 & 1 & 0.7 \\ 0.4 & 0.1 & 0.7 & 1 \end{pmatrix}$. Initial conditions: $Z(t_0) = \begin{pmatrix} 0.05 & -0.02 & 0.0 & 0.0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$, $x_1 = (1,0,0,0)^T$, $x_2 = (0,1,0,0)^T$, $x_3 = x_4 = (0,0,0,0)^T$; $y_1 = (1,0)^T$, $y_2 = (0,0)^T$.

It should be noted that the displayed plot strongly depends on the parameters of the metrices describing the network evolution. By adjusting values of the elements of the matrices we can get different network dynamics. This can correspond to real situation in living organisms when immune system extinct the antigens or it doesn't and there are many of natural parameters regulating immune system dynamics.

In Fig. 2 we plotted the outcome of numerical simulations for the case $\dim X = 4 = \dim Y$. As in the previous case, for simplicity, we consider the matrix D_h being zero. The numerical solution of the dynamical system obtained for certain D_g and D_f also corresponds to the case when interaction between clonal variables X and Y is completely determined by matrices D_g and D_f and, namely, they change the adaptive interaction of the main matrix variables through the matrix variable Z. Examination of the solutions obtained reveals that dynamics of the diagonal elements of the matrices X and $Y \in End\mathbb{R}^4$ - a) and b) and traces of these matrices c) is essentially nonlinear. After some quasi-stationary dynamics of the traces we have their sharp flips to new integer values. During the system evolution a new increase or decrease of X -components can happen which may change essentially its trace dynamics. For initial conditions we used two dimensional subspace of the matrices X and Y. Concerning inhibitor X we chose arbitrary orthogonal vectors $x_{1,}x_2$ and concerning activator vectors we chose two orthonormal vectors. These vectors form matrices X, Y as

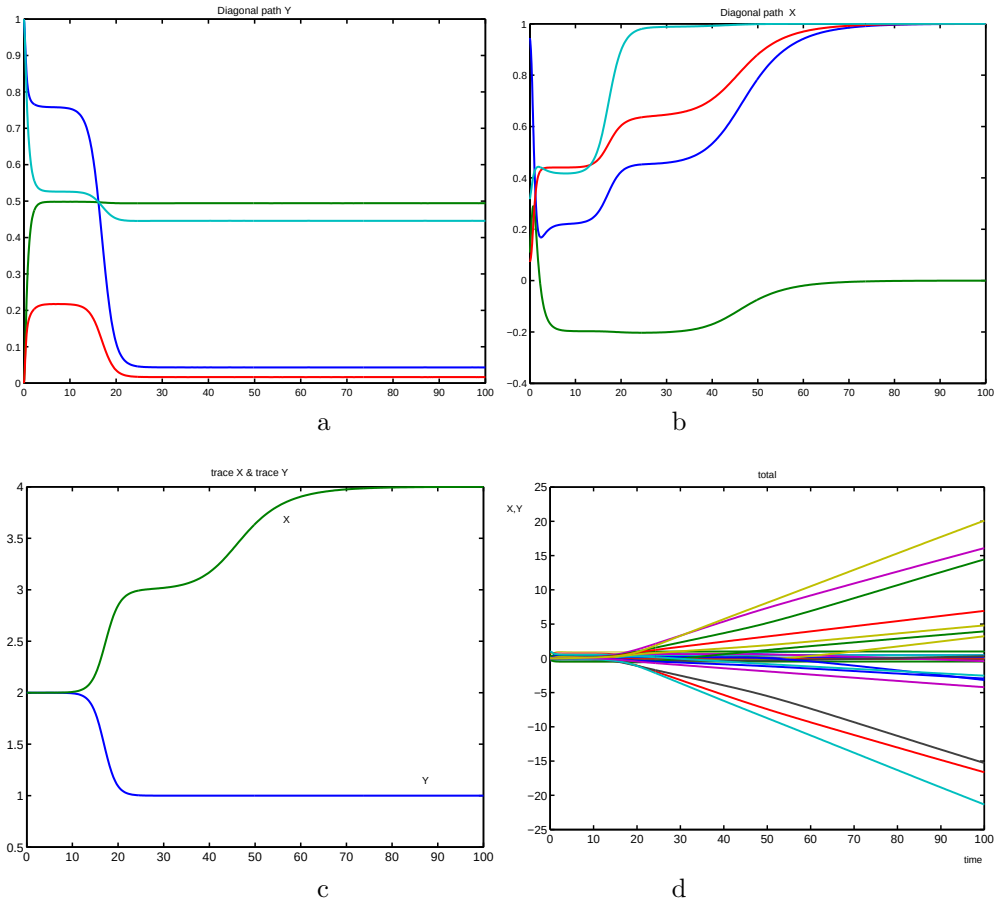


Figure 2: Behavior of the diagonal elements of matrix Y - a), X - b), traces of the matrices X and Y - c), and plot of all solutions of matrices X, Y and Z - d). Here $D_g = -\begin{pmatrix} 1 & 0.5 & 1 & 0.4 \\ 0.5 & 1 & 0.4 & 1 \\ 1 & 0.4 & 2 & 0.5 \\ 0.4 & 1 & 0.5 & 1 \end{pmatrix}$, $D_f = \begin{pmatrix} 0.5 & -0.1 & 0.5 & 0.4 \\ -0.1 & 1 & 0.3 & 0.1 \\ 0.5 & 0.3 & 1 & 0.7 \\ 0.4 & 0.1 & 0.7 & a \end{pmatrix}$, Initial conditions: $Z(t_0) = \begin{pmatrix} 0.0522 & 0.0092 & -0.0040 & 0.0087 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0.0097 & -0.0269 & 0.0086 & 0.0202 \end{pmatrix}$, $X(t_0) = \begin{pmatrix} 0.9448 & 0.1090 & -0.0534 & 0.1937 \\ 0.1090 & 0.6655 & -0.2193 & -0.4033 \\ -0.0534 & -0.2193 & 0.0726 & 0.1280 \\ 0.1937 & -0.4033 & 0.1280 & 0.3172 \end{pmatrix}$, $x_1 = (0.9262, -0.1382, 0.0276, 0.3497)^T$, $x_2 = (0.2948, 0.8040, -0.2680, -0.4415)^T$, $x_3 = (0,0,0,0)^T$, $x_4 = (0,0,0,0)^T$; $y_1 = (1,0,0,0)^T$, $y_2 = y_3 = (0,0,0,0)^T$, $y_4 = (0,0,0,1)^T$.

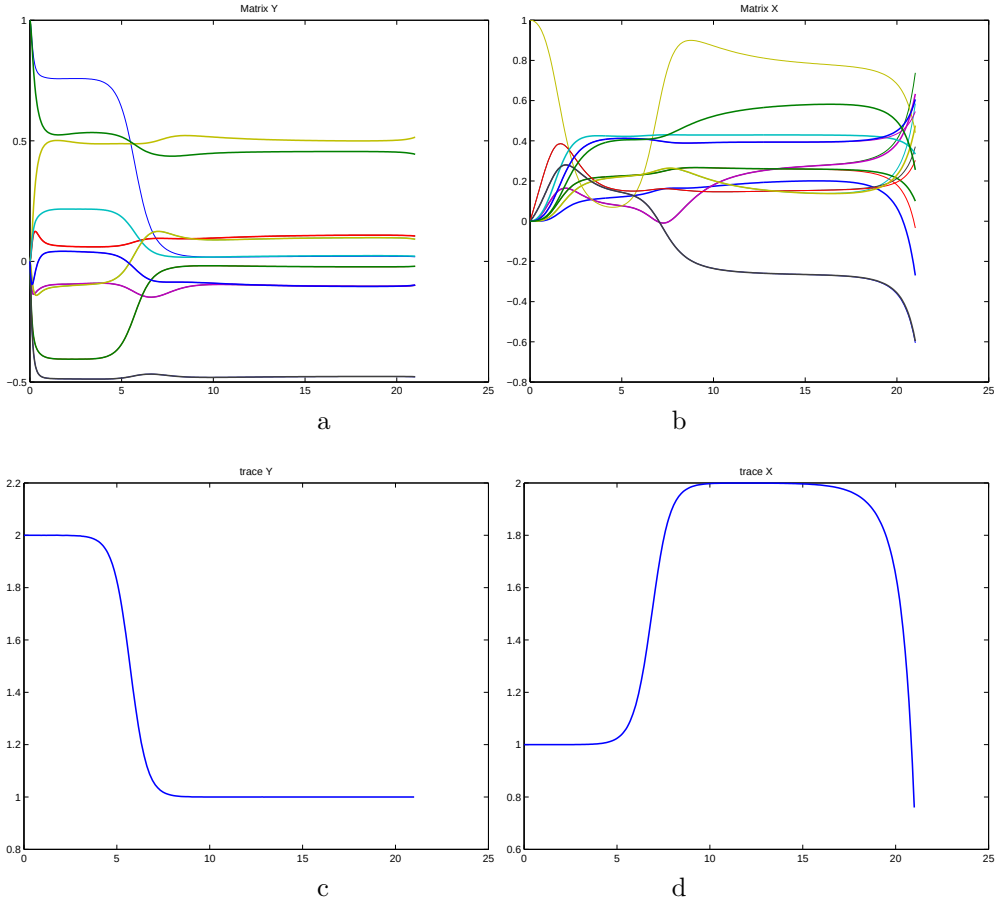


Figure 3: Clonal immune system dynamics for matrix Y - a), for matrix X - b), Trace of the matrices X and Y - c), d correspondingly. Here $D_g = -3\begin{pmatrix} 1 & 0.5 & 1 & 0.4 \\ 0.5 & 1 & 0.4 & 1 \\ 1 & 0.4 & 2 & 0.5 \\ 0.4 & 1 & 0.5 & 1 \end{pmatrix}$, $D_f = \begin{pmatrix} 0.5 & 0 & 0.5 & 0.4 \\ 0 & 1 & 0.3 & 0.1 \\ 0.5 & 0.3 & 1 & 0.7 \\ 0.4 & 0.1 & 0.7 & a \end{pmatrix}$, $D_h = -\begin{pmatrix} 0.3 & 0.6 & 0.2 & 0.9 \\ 0.5 & 1 & 0.03 & 0.4 \\ 0.2 & 0.5 & 0.1 & -0.5 \\ -0.5 & 0.03 & 0.04 & 1 \end{pmatrix}$, Initial conditions: $Z(t_0) = \begin{pmatrix} 0.0 & 0.2 & 0.0 & 0.0 \\ 0.0 & 0.0 & 0.0 & 0.0 \\ 0.0 & 0.0 & 0.0 & 0.0 \\ 0.0 & -0.3 & 0.0 & 0.0 \end{pmatrix}$, $x_1 = x_3 = x_4 = (0,0,0,0)^T$, $x_2 = (0,1,0,0)^T$, $y_1 = (1,0,0,0)^T$, $y_2 = (0,1,0,0)^T$, $y_3 = y_4 = (0,0,0,0)^T$.

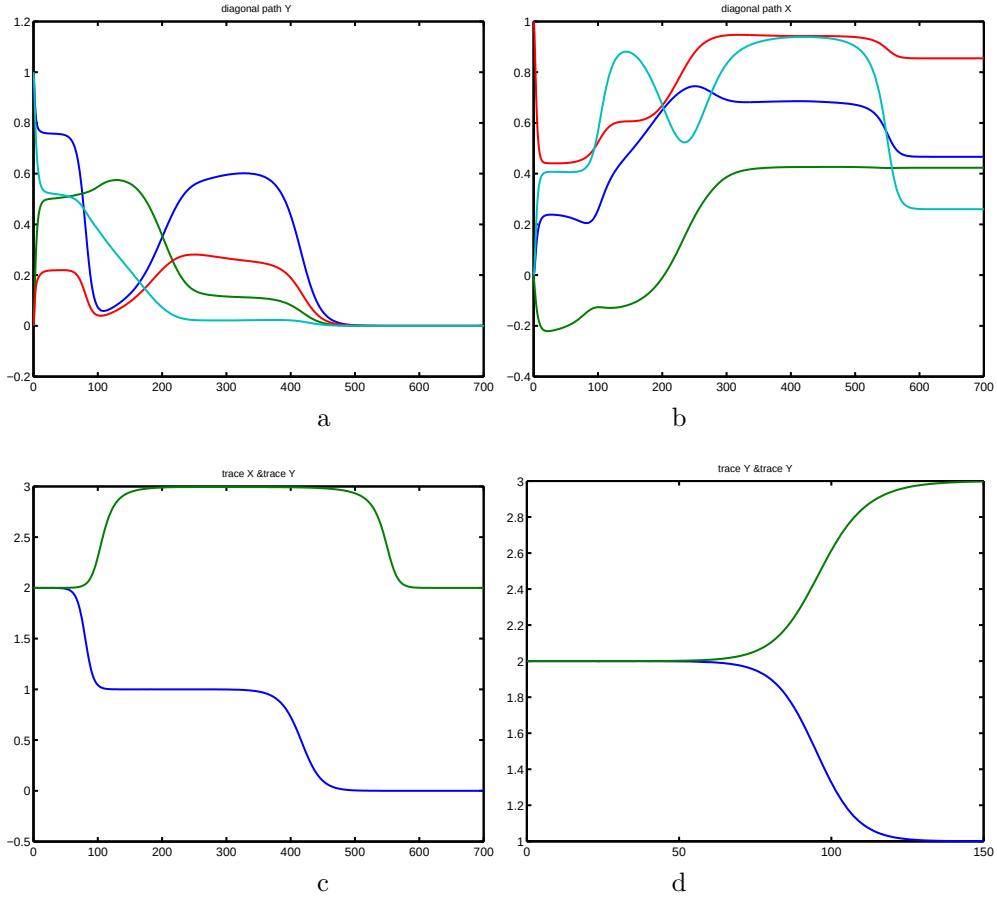


Figure 4: The behavior of the diagonal elements of the matrix Y - a) and X - b). Traces of the matrices X and Y for indexes (1) and (2) - c), d) correspondingly.

Here $D_g = -0.2\begin{pmatrix} 1 & 0.5 & 1 & 0.4 \\ 0.5 & 1 & 0.4 & 1 \\ 1 & 0.4 & 2 & 0.5 \\ 0.4 & 1 & 0.5 & 1 \end{pmatrix}$, $D_f = 0.2\begin{pmatrix} 0.5 & 0.15 & 0.5 & 0.4 \\ 0.15 & 1 & 0.3 & 0.1 \\ 0.5 & 0.3 & 1 & 0.7 \\ 0.4 & 0.1 & 0.7 & 1 \end{pmatrix}$, $\beta_g = \begin{pmatrix} 1 & 0.0 & 0.0 & 0.0 \\ 0.1 & 1 & 0.1 & 0.0 \\ 0.0 & 0.0 & 1 & 0.1 \\ 0.0 & 0.0 & 0.0 & 1 \end{pmatrix}$, $\beta_f = \begin{pmatrix} 1 & 0.0 & 0.0 & 0.0 \\ 0.1 & 1 & 0.2 & 0.0 \\ 0.0 & 0.0 & 1 & 0.1 \\ 0.0 & 0.2 & 0.0 & 1 \end{pmatrix}$. Initial conditions: $Z(t_0) = \begin{pmatrix} 0.0 & 0.2 & 0.03 & 0.0 \\ 0.0 & 0.0 & 0.0 & 0.0 \\ 0.0 & 0.0 & 0.0 & 0.0 \\ 0.0 & -0.3 & 0.02 & 0.0 \end{pmatrix}$, $x_1 = x_4 = (0,0,0,0)^T$, $x_2 = (0,1,0,0)^T$, $x_3 = (0,0,1,0)^T$, $y_1 = (1,0,0,0)^T$, $y_4 = (0,0,0,1)^T$, $y_2 = y_3 = (0,0,0,0)^T$.

well at some given values of coefficients $z_{\alpha\beta}$ do the matrix Z. The specific data of these procedure are presented in caption for Figure 2. From the reported plot we can see that nondiagonal phase trajectories (Fig. 2, d) of the matrices X, Y and Z have practically linear behavior and are relatively stable for large values of time ($t \sim 1000$).

In Figure 3 a) we report the numerical simulation of all components of matrices X- a) and Y- b) and corresponding trace dynamics of these matrices X- c) and Y- d) for the case with new initial data and all matrices being nonequal to zero. In particular, we took the rank of the matrix X in initial conditions equal to be constant 1 and that of the matrix Y equal to 2 and initial vectors are standard orthogonal vectors (See Fig. 3).

The form of the matrix D_h plays essential role in interaction of the clonal network. From the reported plot we can see that phase trajectories of activator Y are stabilized at certain value of $t \in \mathbb{R}_+$ and the values of Y practically doesn't change in time. The simulations run until the time when the system either destroys owing computational errors or stabilizes.

In Figure 4 we present the numerical simulation of the diagonal components of matrices X- a) and Y- b) and the corresponding trace dynamics of these matrices -c) for the network dynamics stimulated by combination of two Lyapunov functions (2), (6) and (2), (8). In these cases new matrices in equations are determined as

$$\widetilde{D}_g = k_g D_g + D_g^{(1,2)},\ \widetilde{D}_f = k_f D_f + D_f^{(1,2)}, \widetilde{D}_h = k_h D_h + D_h^{(1,2)}$$

but equations of the clonal dynamics are persist evidently to be the same as (17). The first upper index (1) corresponds to Lyapunov function (6) and the second upper index (2) corresponds to Lyapunov function (8). The results of computer simulations for first index are presented on Figure 4 a-c) and the second one on the Figure 4 - d). In this case the diagonal elements X - a) diagonal elements of matrix Y - b) and traces of these two matrices c) demonstrate a very interesting nonlinear dynamics. For simplicity of representation and in order to grasp some characteristic features of the clonal network dynamics we used practically the same matrices as in the previous simulations. All parameters of matrices D_f, D_g, D_h, $D_f^{(1)} = D_f^{(2)}$ and $D_g^{(1)} = D_g^{(2)}$ are presented on captions to this figure. With our simulations we studied the effects of the combination influence of these two Lyapunov potentials.

It was established within these simulations that coefficients before the medication matrices influence sufficiently the network dynamics. It should be noted that the behavior of the system with Lyapunov potential combinations of these two potentials (2) and (6), (8) are much more stabilized and we have many opportunities by taking coefficients k_g, k_f, k_h small enough to obtain different trace dynamics of the system. Analyzing behavior of the traces describing our immune clonal network we can conclude that small variations of the parameters do not change seriously the clonal dynamics. In this case there exists some region of attraction when the solutions persist the same form. But at some values of elements of matrices these solutions change drastically. This is the

case happening in the real immune system dynamics when inhibitory receptors possess many of parameters which behave precisely in order to depress antigens from the clonal network.

Within our model of an immune clonal system the matrix trace $trY \in \mathbb{Z}_+$ of the matrix Y, being an integer, counts the number of activated excitatory receptors strings at the moment of time $t \in \mathbb{R}_+$ during the interaction of excitatory clonal sub-network with inhibitory clonal sub-network, described at the same moment by the matrix trace $trX \in \mathbb{Z}_+$ of the matrix X, being also an integer and counting, respectively, the number of activated inhibitory receptors strings during the interaction. As one can see, during the interaction between inhibitory and excitatory clones at some moments of time there are switched some new excitatory and inhibitory receptors strings, and further at next whiles of time during their interactions, some of excitatory receptors strings become depressed and some inhibitory receptors either appear or become dis-activated too. This event can be interpreted, for instance, as follows: our inhibitory clonal network solved its immune task to dis-activate the excitatory clonal sub-network, and next at some later while of time becomes idle too, leaving itself in the initial awaiting state.

Thereby, one can state that the model studied in this paper possesses many of properties suitable for possible responses of a real clonal network. The stimulation of the interaction between excitatory and inhibitory sub-systems demonstrates their expectable direct self-similar and complementary behavior. This model is obviously not still completely satisfactory because it needs many of external parameters accounting for the main important features of real clonal network dynamics. But we believe that the work presented in this paper is an alternative step towards better understanding the essence and nature of immune network dynamics. Since the realistic immune networks do involve much more than several receptor strings elements, such an analysis is a new step to a completely novel approach to understanding the functioning of real clonal immune networks.

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