DYNAMICS AND TOPOLOGY OF IDIOTYPIC NETWORKS

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Jerne's idiotypic network was previously modelled using simple proliferation dynamics and a homogeneous tree as a connection structure. The present paper studies analytically and numerically the genericity of the previous results when the network connection structure is randomized, e.g. with loops and varying connection intensities. The main feature of the dynamics is the existence of different localized attractors that can be interpreted in terms of vaccination and tolerance. This feature is preserved when loops are added to the network, with a few exceptions concerning some regular lattices. Localized attractors might be destroyed by the introduction of a continuous distribution of connection intensities. We conclude by discussing possible modifications of the elementary model that preserve localization of the attractors and functionality of the network.

1. Introduction. Since the proposal of an immune network by Jerne (Jerne, 1974), a number of mathematical models have been suggested to describe the idiotypic network, see references in Perelson (1988) and Atlan and Cohen (1989). Recent models are based on large systems of differential equations, which represent the time evolution of lymphocyte populations and antibody concentrations. Their aim is to describe the generic dynamical properties of the network, in terms of the attractors of the dynamics. These attractors are interpreted as functional properties of the immune system such as vaccination, tolerance and auto-immune disease.

One of the simplest connection structures that can be used to represent the network is the Cayley tree (Weisbuch et al., 1990), rendering the model completely soluble (Neumann and Weisbuch, 1992). We have previously studied the dynamics of this model, to be further referred to as the WBP model, determining which attractors are reached as a function of the parameter set-up. However, the connectivity of the mammalian immune network, although mostly unknown, is certainly not that of a homogeneous Cayley tree. The purpose of the present paper is to treat the case of a more general connectivity, starting from the methods and the ideas that were developed in our previous studies of Cayley tree networks (Weisbuch et al., 1990; Neumann and Weisbuch, 1992).

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Let us recall the main simplifications of the WBP model:

- The topology of the network is reduced to a *homogeneous Cayley tree* (see Fig. 1), where all interactions are of *equal intensity*.
- All different cell types, of the same idiotype, are clumped together into *one variable* and its dynamics are studied.

![Homogeneous Cayley tree structure](image)

Figure 1. Scheme of the homogeneous Cayley tree structure, shown for $m = 3$. Each clone, except the root which is the idiotype that recognizes the antigen, is connected to one ancestor ($m_a = 1$) and two successors ($m_r = 2$). All affinities are equal, $J_{ij} = 1$.

We refer the reader to DeBoer *et al.* (1991), Perelson and Weisbuch (1992) and Segel and Perelson (1991) for discussion on the effect of having different antibody and cell dynamics, which remove the second simplification.

The purpose of the present paper is to study the case where the first assumption, the homogeneous Cayley tree topology, is removed. First we have no reason to suppose that all connection strengths are identical. Furthermore, standard interpretation of recognition based on complementary shapes implies a network with loops. For instance, similarity between idiotypes and their anti-anti-idiotypes implies that if two anti-idiotypes (Ab2) recognize the same idiotype (Ab1), its "mirror" image anti-anti-idiotype (Ab3) might also recognize the same two anti-idiotypes, hence forming a loop (see the $J_{32}$ loop in Fig. 5) that includes Ab1, the two Ab2’s and Ab3.

We possess powerful simulation tools and analytical methods that allow us, at least in principle, to compute which attractor is reached for any random net under any specific antigen presentation and parameter set-up. What we are now seeking is some insight into the role of loops and non-homogeneity of connections on the nature and the attainability of attractors.

A change of attractor by the system under the influence of antigen presentation is interpreted as a memory of the system. One of the most exciting