# A dynamical view on long-term-potentiation

**Frido Erler, Michael Meyer-Hermann and Gerhard Soff**
Institut für Theoretische Physik, TU Dresden

Our task is a quantitative description of neuron dynamics. Especially we pointed our attention on neuronal systems which have the capability of learning, i.e. which undergoes long lasting behavioral changes in dependences on input data induced on a relatively short time scale. One very important effect in this context is long-term-potentiation (LTP), which is already observed in neuronal systems containing only two participating neurons related by chemical synapses. If one compares the slope of the excitatory postsynaptic potential (epsp) due to a simple action potential induced in the presynatic neuron before and after initiation of LTP, one finds a great enhancement of the epsp, indicating a higher sensitivity of the long term potentiated synapse. This enhancement lasts for hours, days or even months and is initiated by a specific set of presynaptic action potentials (tetanus) in less than 1s. Experimentally LTP is well measured in different neuronal systems and its induction is well under control. However, an understanding of the expression of LTP, i.e. to find the long lasting changed feature(s) of the participating neurons responsible for the enhanced epsp, is still missing. Even a clear statement about the location of LTP-expression — pre- or post-synaptic or an additonal interaction between both — is not possible yet.

We want to give a contribution to the current discussion using more quantitative arguments. Using reaction-diffusion equations, the emergence of the effect is modeled in a pure dynamical way, i.e. it is analyzed if key quantities of LTP embody the possibility of producing the effect solely out of their dynamic interdependence. The used dynamical variables are for example the calcium concentration relevant for transmitter release and the rates of exo- and endo-cytosis. The work is accompanied by the setup of a simulation program written in C++. In both methods our attention lies on the predictive power of the models: Only experimentally fixed parameters are used. Exactly at this point lies the principal value of our Ansatz and at the same time the main difficulty, as the different existing experimental bounds on the parameters are established on different systems with a questionable degree of comparability. So a large part of our work is contributed to disentangle the existing data towards a coherent set of parameter values.

If such a procedure became successful, we would be able to analyse, which parts of LTP induction and expression are necessary or optional from a dynamical point of view. This may leed to a contribution towards a destillation of the elementary ingredients for LTP.

# Germinal Center Dynamics

**Gianaurelio Cuniberti, Andreas Deutsch, Michal Or-Guil**
MPI für komplexe Systeme, Dresden

**Michael Meyer-Hermann**
Institut für Theoretische Physik, TU Dresden

A humoral immunity response shows a lot of interesting features. The presentation of a specific antigen leads to the activation of a set of B-cells. In an early phase of immunity response these may differentiate to antibody producing cells which bind to the presented antigen-epitops with a certain affinity. Alternatively, the activated B-cells proliferate with a high rate in the environment of follicular dendritic cells and develop to germinal centers. These are not only able to give rise to a later immunity response mediated by antibody-producing plasma-cells. The affinity of these antibodies to the presented antigen is optimized. Finally the germinal center environment plays an important role for the differentiation of memory B-cells, which control the secondary humoral immunity response.

Germinal centers are built up polyclonally, i.e. a very little number of activated B-cells is developping to one germinal center. These few B-cells are of a specific phenotype with a given affinity to the activating antigen. The very high proliferation and hypermutation rates for centroblasts in germinal centers leads to a broadening of specifity in the phenotype space. On the other hand the highly specific selection process in the light zone of the germinal center allows an optimization of the affinity to the antigen. The nonselected cells die through apoptosis, while apoptosis is inhibited in the case of a positive selection.

We describe these dynamics by an appropriate set of differential equations, reducing the model to the essential variables. From this starting point we have the possibility to examine the influence of single quantities on the behavior of the germinal center. As we exclusively use experimentally fixed parameters, this model gains predictive power and — besides giving bounds on possible values for the used quantities — it may help to find criterions how the selection process is choosen optimally. This question is of relevance for the flexibility or tolerance of the immune response against mutation of the antigen. So their should exist an optimal equilibrium of specifity and diversity of the immune response in the phenotype space.

Another open problem is the dimension and the largeness of the phenotype space. As there is a great amount of experimental data available, we hope to be able to fix all of the parameters entering our model and by this way to fix the dimensions of the phenotype space. If such a procedure is successful in the case of the germinal center, the question of the universality of these results emerges naturally. Highly connected to this problem is the relation of genotype and phenotype spaces. One single mutation may leed to very different jumps in the corresponding phenotype space.

Finally we will address our attention to germinal center ensembles, to get a realistic model of a complete humoral immune response after exposure to a specific antigen.