

## Virtual Antigens made by Laser Beams

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Virtual antigens are electrodynamic structures that are able to attract real molecules (antibodies, viruses, bacteria, messenger molecules etc.) like recombinant antigens. These virtual structures can be used for medical diagnostics, development of therapeutic antibodies and analysis of messenger molecules.

The scientific basis for the development of virtual antigens is a theory of electrodynamic interaction (Electrodynamic Binning Theory) between antibodies and antigens, which is similar to the lock and key principle, but the theoretical model is based on electrodynamic interaction instead of chemical interaction. Electrostatics has a big importance in immunology (electrophoresis) but electrostatics is ignored currently in a state of the art life science. We think the reason for this is that electrostatics can be understood without mathematics, to understand electrostatics a deep understanding of electromagnetic field theory (Maxwell's equations) and tensor differential equations (linear and non-linear) up to a rank of 1500000 is required. The complexity of mathematics is comparable to mathematics in astrophysics or quantum mechanics. So electrostatics of molecules requires a multidisciplinary approach to explain immunological effects in a mathematical form.

In 1894 Emil Fischer described the lock and key principle for the interaction between enzymes and substrates. After finding that this theoretical model cannot describe the chemical interaction between enzymes and substrates correctly, D. E. Koshland developed in 1958 the concept of induced fit [1]. This is the currently valid model for describing the specific interaction between antibodies and antigens. One problem with this concept is that it cannot explain the energy source for this induced fit process. Another problem is that x-ray crystallization showed that the contact area between antibody and antigen is relatively flat [2]. Also only 30% of each antibody CDR are in contact with the antigen [2]. And so the authors [2] concluded that other effects as electrostatics must play a role in the binding process between antibody and antigen. But they did not think on electrostatics, which is the dynamic form of electrostatics.

Making kinetic measurements of the interaction between highly specific antibodies and antigens we found that kinetics is in contrast to the law of mass action if the antibody is not labeled but it is in accordance with the law of mass action if the antibody is labeled with a 40 nm gold particle [3]. This can also not be explained with a direct chemical contact between antibody and antigen. Alexandre Rothen [4] found in 1946 that buried antigens are attracting antibodies. Analyzing his measurement results [4] we found that the attraction of a buried antigen monolayer is smaller than the attraction of the antigen monolayer at the surface. But it can be calculated that the attraction per monolayer is in accordance with electrostatic or electrodynamic field strength theory. From this point of view attraction of antigens cannot be done by chemical effects it must be done with electromagnetic effects. Specificity cannot be reached with electrostatic effects but with electrodynamic effects. To exclude chemical effects we have put a 7nm Si<sub>3</sub>N<sub>4</sub>-membrane between antibodies and antigens and found that antibodies are still attracted by antigens [5].

So we developed a theory for the electrodynamic interaction of antibodies and antigens and made a mathematical proof of principle

[3]. Additional to this we have produced a trick film to explain the physical principle [6]. This trick film is also used in physics to explain students the laws of conservation of energy and momentum.

With the same physical model and existing knowledge of the molecular structure we developed a theory for the interactions between virus and target, bacterium and target, enzyme and substrate, cell and target and movement of dendritic cells. Additional to this we have developed a model for communication of messenger molecules. We think they are also using electrodynamic effects [7].

For creating electrodynamic effects we generally need mechanical springs, molecular masses and electrical charges in the molecules. We think in accordance with other researchers [8-11] that beta sheets are linear springs and alpha helices are progressive springs [12]. Additional to this our theory [3] requires that the hinge region of the antibody acts also as a spring. So the hinge region of an antibody has an influence on the affinity of the antibody. That means that a high affinity antibody which is optimized for an antigen can have a higher affinity than its Fab-fragments. This effect was found by Hudson and Kortt in 1999 [13]. The elasticity and mass of the hinge region explain also that scFv-single chain antibodies are working only with a definite linker size. The linker must replace the spring and the mass of the hinge-region of a full size antibody for getting high affinity. From our theory each CDR of a symmetric antibody can have specificity to a different antigen. This effect was found by Chen [14]. She has produced symmetrical antibodies where the light and heavy chains have an affinity to different antigens.

According to our theory there must be a molecular twist in the antibody structure so that it can rotate. This twisting was also found [15] but in contrast to the shown rotation [15] the antibody would rotate in accordance with our theory in the opposite direction.

Our virus-target theory is a little bit more complex than our antibody theory but it can also be calculated with mathematics. A virus with for example 1500 epitopes can be calculated by non-linear tensor differential equations of rank 1500. Our bacterium/cell-target theory requires the solution of a non-linear tensor differential equation of rank 1500000 if 1.5 million epitopes are on the membrane surface. The lipid bilayer acts as a coupling spring between epitopes. It enables the energy transfer between epitopes.

Viruses and bacteria are emitting both a high frequency signal in

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the THz range and a low frequency electromagnetic signal if no target is present. American scientists have started a project to measure THz waves of a virus [16] to identify outbreak of the virus. Peter Ortoleva [16] has found these THz waves of a virus predicted by us in 2011 [17] in 2013 and he is sure that the THz-signals are coming from the virus [18]. His expectation is consistent with our antibody-antigen theory [3] and our virus-target theory which was published in simplified form in August 2011 as a trick film [17].

The low frequency signal (coupling frequency of epitopes via lipid bilayers) disappears if a target is in the reach of the virus or bacterium. The low frequency signal is detectable with an antenna and a spectrum analyzer. It is comparable with the  $\omega_1$ - $\omega_2$  frequency of our antibody theory [3]. We have found this low frequency signal and also Luc Montagnier has found such a signal [19,20]. He thought that the signal is coming from DNA. But according to our theory the signal must come from the membrane of a virus or bacterium. And the signal frequency is according to our theory higher for a virus compared to a bacterium. This was also measured by Montagnier.

We have developed a closed model for proteins, messenger molecules, antibodies, viruses, bacteria and cells that are consisted with observed effects. According to our theories the interaction is based on electrodynamic effects. The advantage of our theory is that the interaction of molecules is mathematically calculable. In contrast to chemical interaction electrodynamic effects are working with light speed and they are very safe, chemical interaction would be significantly slower and very unsure.

Virtual antigens can be used for medical diagnostics. We are expecting that we can produce  $10^8$  different virtual epitopes/antigens. For each real antigen we can theoretically create a similar virtual epitope/antigen. So if an antibody binds to a virtual antigen we can analyze to which real protein, virus, bacterium or cell it would bind.

But the technique can not only be used for medical diagnostics, it can also be used for optimizing therapeutic antibodies. Scanning the target of a therapeutic antibody with all  $10^8$  virtual antigens and afterwards scanning the antibody itself it can be seen how to change the CDR's of the antibody to get a working therapeutic antibody. The scan gives information if the antibody is polyspecific or not and how to change each single CDR to get a monospecific antibody with no harmful side effects. The calculation of the required CDR-changes is given by special software.

All found experimental data are consistent with our theory, so we think it is true. At the moment there is no scientific argumentation against our theory.

We think that electrodynamics is not only used by the immune system, we expect that it is a general principle in cells. So we think electrodynamics can also be used to explain the physical principle of autoimmune diseases and Alzheimer.

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