Untangling the biological hairball of immune recognition networks

Complex mathematical models of interaction networks are routinely used for prediction in systems biology. However, it is difficult to reconcile network complexities with a formal understanding of their behavior. I will introduce several models of immune recognition by T cells and will show how a simple procedure can be used to reduce them to functional submodules, using statistical mechanics of complex systems combined with a fitness-based approach inspired by in silico evolution. Our procedure works by putting parameters or combination of parameters to some asymptotic limit, while keeping (or slightly improving) the model performance, and requires parameter symmetry breaking for more complex models. An intractable model of immune recognition with close to a hundred individual transition rates is reduced to a simple two-parameter model, and connected to the “adaptive sorting” principle that we previously identified and experimentally validated. Our procedure extracts three different mechanisms for early immune recognition, and automatically discovers similar functional modules in different models of the same process allowing for model classification and comparison.