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Analysis of p53 transactivation on different Response Elements

p53 is the guardian of the genome, it acts as a transcription factor regulating the production of several proteins upon DNA damage. Maybe this is the most investigated protein in human cells, still the exact mechanism how p53 binds to response elements (REs) in the DNA is still unclear. A yeast-based essay enables us to investigate its binding dynamics to REs of highly important targets. We collected time courses of transcriptional activity at various REs by measuring luminescence induced by p53 regulated promoters at various p53 induction levels. We created a mathematical model for the molecular interactions of p53 dimers and their binding to REs. Alternative versions of the model contain possible proposed binding orders and interactions. We perform large scale parameter estimation to identify which model can give such parameter sets that fits the experimental measurements. Initial results revealed that earlier time points need to be measured to allow proper fitting. We observed that, some parameters show low sensitivity at all p53 induction levels. Thus we narrowed down on a subset of parameters from the initial set and run the estimation by fitting all the measured REs together and observed the intra RE and inter RE variations in the parameters. With the parameter estimation we plan to identify the details of p53 RE binding events. The emerging modeling results will be further validated experimentally.