Modelling a gene regulatory network for floral cell fate determination in Arabidopsis

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1 Introduction

Project goal is the development of a gene regulatory network that dynamically describes protein concentrations in the different floral organs in Arabidopsis Thaliana.

Floral organ identity is determined by differential expression of cell fate determining proteins. This is described in the ABC model, which is based on the actions of five types of MADS proteins, [3].

After floral induction, the stem cells in the Shoot Apical Meristem (SAM) differentiate into the four different floral organs: petals, sepals, stamens and carpels. The exact initial trigger of this differentiation and how this gives rise to the expression of the ABC genes, is unknown. It is assumed that the hormone auxin, in interplay with the genes, plays an important role [1]. Every plant cell contains a regulatory network of ABC type genes that regulates the protein concentrations towards the concentrations associated with the profiles described in the ABC model, see for example [2].

An effort is made to develop a dynamical model for the flower network, starting from the point that the primordial are formed and cell differentiation starts. This model should give a quantitative as well as qualitative description of gene expression evolution inside the flower organs.

2 Method

A small network of six genes is proposed, together with logical rules for the gene interactions, based on literature [2]. These logical rules were inserted into a boolean network, describing for each gene an expression level of either 1 (on) or 0 (off). In this network, all possible initial concentration profiles (2^6 profiles) indeed converge to the four expression level patterns of the organ identity genes that are predicted by the ABC model, without limit cycles. Hence, this network seems to contain a qualitatively correct topology. However, we expect that more processes play a role. For example, in [2] a model consisting of 15 genes was used to predict cell fate. To extend the analysis, we develop a continuous-time network consisting of ordinary differential equations (ODE's) with the same topology and gene interactions as the boolean network. The ODE network describes the evolution of protein concentrations, and will give more information on the quality of the chosen model structure (see Discussion).

The ODE model has three different mechanisms. First, gene regulation is described by Hill functions, which account for promotion or repression by proteins or protein complexes. Second and third, each protein has a production- and a decay rate. These mechanisms together introduce 30 parameters that have to be estimated from a small set of 48 experimental data points. The estimation problem is nonlinear, which is generally laborious due to the occurrence of local minima. Following the method in [4], we transform the problem into a linear least squares problem with constraints. The constraints are based on realistic parameter ranges from literature.

3 Discussion

The estimation error (the residuals) indicate the reliability of the chosen model structure. Large residuals can be caused by a lack of essential genes, or an incomplete topology. If the residuals are small, the model structure and the estimated parameters can be considered realistic. With a suitable ODE model it is possible to determine the domains of attraction of the steady states in terms of protein concentrations, which can help by modelling the mechanism that initiates cell differentiation. The results of the estimation algorithm will be presented during the symposium.

References

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