Supplementary Material
Network Simplification

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Boolean GRNs are useful to study the complex logic of transcriptional regulation involved in cell
differentiation. However, a comprehensive understanding of the mechanisms participating in cell fate
dynamics must take into account the continuous character of the variables involved in the description:
levels of genetic expression, differences in concentrations, in decay rates, threshold expression values,
etc. These factors may be taken into account by translating the discrete dynamical mappings
describing GRN interactions into a set of differential equations. In order to get formal consistency
of both descriptions, the new variables and operators that constitute the logical propositions must
satisfy a generalization of Boolean axiomatics into the continuous realm. For that purpose, we
transform the logical connectors and, or, and not according to the following operations:

\[ a \text{ and } b \rightarrow a \cdot b \quad a \text{ or } b \rightarrow a + b - a \cdot b \quad \text{not } b \rightarrow 1 - b. \]  \hspace{1cm} (1)

It is straightforward to show that these rules satisfy the axioms of Boolean algebra. We may then
transform the Boolean logical propositions by direct substitution. An example is given by:

\[ (a \text{ or } b) \text{ and not } c \rightarrow [a + b - a \cdot b] \ (1 - c). \]

We now consider the following set of differential equations defined by step-like inputs \( \Theta[w_i] \),
where \( w_i \) is a continuous logical proposition:

\[ \frac{dx_i}{dt} = \Theta[w_i(x_1, ..., x_n) - \theta_i] - \alpha_i x_i. \]  \hspace{1cm} (2)

Here, \( \theta_i \) is a threshold value (usually, \( \theta_i = 1/2 \)), while \( \Theta[w_i(x_i - \theta_i)] \) is a logistic functional whose
value is 1 if \( w_i > \theta_i \), 1/2 if \( w_i = \theta_i \), and 0 if \( w_i < \theta_i \). \( \alpha_i \) represents the decay rate for the expression
of node \( i \). A representation of \( \Theta[w_i] \) is

\[ \Theta[w_i] = \frac{1}{\exp[-\beta(w_i - \theta_i)] + 1}, \]  \hspace{1cm} (3)

where \( \beta \) is a saturation rate. For \( \beta \gg 1 \), the functional \( \Theta[w_i] \) becomes a Heaviside step function:
\( \Theta[w_i - \theta_i] \rightarrow H[w_i - \theta_i] \).

It may be shown that when all \( \alpha_i = 1 \), the steady states of the set (2), defined by \( dx_i/dt = 0 \),
coincide with attractor set provided by the discrete Boolean approach, indicating the robustness of
the continuous analysis.
Figure 1: Differentiation and plasticity of CD4+ T cells in the continuous model. (A & B) Differentiation of Treg cells in response to IL2e, TGFBe and IL21e in the micro-environment. (C & D) Transition from Treg to Th17 in response to perturbations in IL2e.