# Prediction of Debacle Parts for Robustness in a Cell by using Recurrent Neural Networks

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## 1 Introduction

Living organisms have sophisticated control mechanisms to keep biological system robust against abnormalities from inside/outside of them. However, at the same time, the control mechanism has a critical point at which the stability can be broken easily. This paper proposes a method to find critical points of the control mechanism in a biological pathway described by hybrid functional Petri net (HFPN)[1, 3]. Since, in order to find critical points generally, it is necessary to remove an arc of HFPN one by one, the computational time for performing this is extremely rich. In our method, an HFPN is converted to the recurrent neural network (RNN), knocking out connections of the RNN, checking robustness of the biological pathway with the RNN, and finding some crucial points for the robustness [2]. With the RNN which have learned the behavior of HFPN, we can find out a critical point immediately. Examples to apply this method to a circadian clock genetic mechanism and an apoptosis pathway [4] are presented.

## 2 Prediction of Debacle Parts for Robustness

Our prediction method consists of two stages. The first stage is the process which converts a biological pathway from HFPNs to RNNs. Correspondences of RNNs for a simple pathway described by HFPN (the upper left part of Figure 1) are shown in the upper center part of Figure 1. Conections are performed as follows:

1. Tokens extracted from places of an HFPN are used as input signals for input units of RNN.
2. Places and transitions of HFPN correspond to hidden units (including output units) of RNN.
3. Arcs between places and transitions correspond to connections between units of RNN.

By back propagation through time (BPTT) method, the RNN learns behaviors of HFPN until errors are going to be constant in the local minimum.

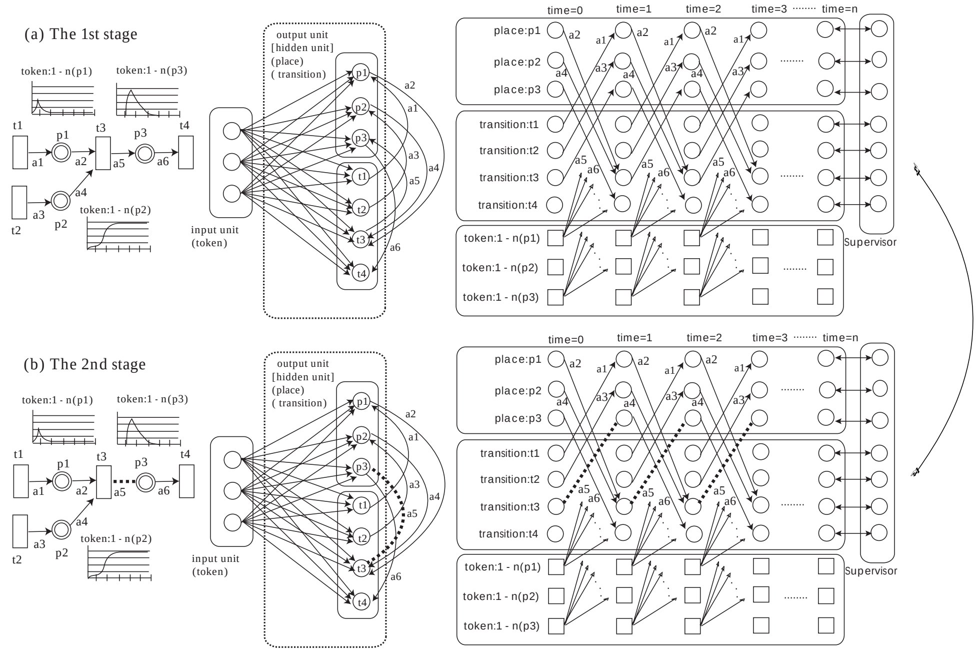


Figure 1: (a) The process which converts a biological pathway from HFPNs to RNNs, (b) The process knocking out boundings of learned RNNs

The next stage is the process knocking out bondings of learned RNNs one by one. The relationships among these are depicted in the lower part of Figure 1. The lower left part of Figure 1 shows an example knocking out the arc `a5` connected from the transition `t3` to the place of `p3` in HFPN. This action is equivalent to the action removing connection from the unit of `t3` to the unit of `p3` of RNNs (the lower center part of Figure 1). Therefore, in the RNN decomposed by the BPTT method, the connection from the transition `t3` to the place `p3` was deleted at any time (the lower right part of Figure 1). Next, errors are calculated by comparing the output units before knocking out with the output units after knocking out. When the amount of errors is large, it can be considered that the influence of knockout is large and that the corresponding biological pathway is related to a critical point for robustness. Prediction of debacle parts for robustness is attained by repeating this processing for all conection of RNNs.

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