

Supplemental material for the IJDMB paper

1 Experimental validation

In this section we describe two proof-of-concept experiments for the analysis of a real interaction network. First, we take the dynamical network model of the *Budding Yeast* network described in Li et al. (2004), and translate it to our framework. The structure of the network is depicted in Figure 1. The authors report that the network has 7 attraction basins and 7 stable states. The second experiment involves the modelling of the *Fission Yeast* network described in Davidich & Bornholdt (2008). The structure of the network is depicted in Figure 2. The authors of Davidich & Bornholdt (2008) report that the network contains 12 stable states as well as 1 stable cycle consisting of 3 states.

We build a general framework for both networks, although as it was mentioned in Section ??, the Budding Yeast network does not require the concept of threshold and thus does not require rules G2.2, G3.2, G7, G7.1, G8, G8.1. We build the framework from the following rules: G1, G2¹, G2.1, G2.2, G3¹, G3.1, G3.2, G4¹, G5, G6, G7, G7.1, G8, G8.1, G9, G10. Recall that this set of rules defines the general network semantics that is independent of any particular network.

1.1 Budding Yeast network

The structure of the Budding Yeast network, depicted in Figure 1 is captured by means of the following S-rules:

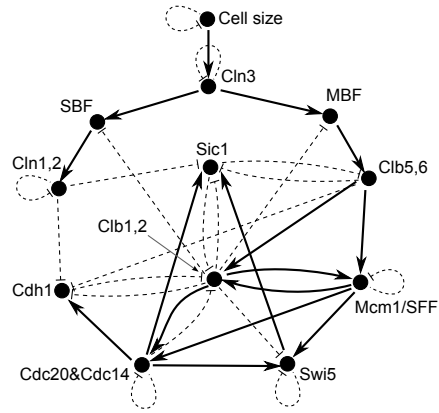


Figure 1: The dynamical network model of the *Budding Yeast* cell cycle. Taken from Li et al. (2004).

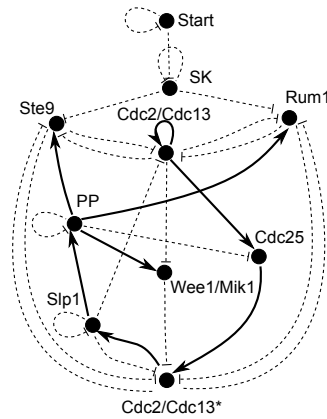


Figure 2: The dynamical network model of the *Fission Yeast* cell cycle. Taken from Davidich & Bornholdt (2008).

<i>protein(cln3).</i>	<i>protein(clb56).</i>
<i>protein(sbf).</i>	<i>protein(cdh1).</i>
<i>protein(mbf).</i>	<i>protein(clb12).</i>
<i>protein(cln12).</i>	<i>protein(mcm1).</i>
<i>protein(sic1).</i>	<i>protein(cdc20).</i>
<i>protein(swi5).</i>	
<i>inhibits(cln3, cln3, T).</i>	<i>inhibits(cdc20, cdc20, T).</i>
<i>inhibits(cln12, cln12, T).</i>	<i>inhibits(mcm1, mcm1, T).</i>
<i>inhibits(sic1, clb56, T).</i>	<i>inhibits(clb12, swi5, T).</i>
<i>inhibits(clb56, sic1, T).</i>	<i>inhibits(clb12, cdh1, T).</i>
<i>inhibits(sic1, clb12, T).</i>	<i>inhibits(cdh1, clb12, T).</i>
<i>inhibits(clb12, sic1, T).</i>	<i>inhibits(cdc20, clb12, T).</i>
<i>inhibits(cln12, sic1, T).</i>	<i>inhibits(cdc20, clb56, T).</i>
<i>inhibits(clb12, sbf, T).</i>	<i>inhibits(clb56, cdh1, T).</i>
<i>inhibits(clb12, mbf, T).</i>	<i>inhibits(cln12, cdh1, T).</i>
<i>inhibits(swi5, swi5, T).</i>	
<i>activates(cln3, mbf, T).</i>	<i>activates(mcm1, cdc20, T).</i>
<i>activates(cln3, sbf, T).</i>	<i>activates(swi5, sic1, T).</i>
<i>activates(mbf, clb56, T).</i>	<i>activates(cdc20, swi5, T).</i>
<i>activates(clb56, mcm1, T).</i>	<i>activates(cdc20, sic1, T).</i>
<i>activates(clb56, clb12, T).</i>	<i>activates(cdc20, cdh1, T).</i>
<i>activates(mcm1, clb12, T).</i>	<i>activates(clb12, cdc20, T).</i>
<i>activates(clb12, mcm1, T).</i>	<i>activates(sbf, cln12, T).</i>
<i>activates(mcm1, swi5, T).</i>	

There are 11 proteins, 19 inhibiting and 15 activating reactions in total, each modelled with an S-rule.

1.2 Fission Yeast network

The structure of the Fission Yeast network, depicted in Figure 2 is captured by means of the following S-rules:

<i>protein(sk).</i>	<i>protein(cdc25).</i>
<i>protein(ste9).</i>	<i>protein(pp).</i>
<i>protein(rum1).</i>	<i>protein(wee1).</i>
<i>protein(cdc2).</i>	<i>protein(slp1).</i>
<i>protein(cdc2_star).</i>	<i>protein(start).</i>
<i>inhibits(sk, ste9, T).</i>	<i>inhibits(cdc2, wee1, T).</i>
<i>inhibits(sk, rum1, T).</i>	<i>inhibits(ste9, cdc2_*, T).</i>
<i>inhibits(cdc2, ste9, T).</i>	<i>inhibits(slp1, cdc2, T).</i>
<i>inhibits(ste9, cdc2, T).</i>	<i>inhibits(cdc2_*, ste9, T).</i>
<i>inhibits(cdc2, rum1, T).</i>	<i>inhibits(rum1, cdc2_*, T).</i>
<i>inhibits(rum1, cdc2, T).</i>	<i>inhibits(cdc2, rum1, T).</i>
<i>inhibits(pp, cdc25, T).</i>	<i>inhibits(slp1, cdc2_*, T).</i>
<i>inhibits(wee1, cdc2, T).</i>	<i>inhibits(slp1, slp1, T).</i>
<i>inhibits(sk, sk, T).</i>	<i>inhibits(pp, pp, T).</i>
<i>activates(cdc2, cdc25, T).</i>	<i>activates(slp1, pp, T).</i>
<i>activates(pp, ste9, T).</i>	<i>activates(cdc25, cdc2_*, T).</i>
<i>activates(pp, rum1, T).</i>	<i>activates(cdc2_*, slp1, T).</i>
<i>activates(pp, wee1, T).</i>	
	<i>inhibition_level(cdc2_*, -1).</i>
	<i>activation_level(cdc2, -1).</i>

There are 10 proteins, 18 inhibiting and 7 activating reactions in total, each modelled with an S-rule.

Some facts such as the activation threshold of *Cdc2/Cdc13* or the inhibition threshold of *Cdc2/Cdc13** are not explicitly seen on the network in Figure 2; to figure out the exact execution flow one has to read the corresponding article Davidich & Bornholdt (2008). This shows the implicit advantage of an ASP model in comparison with boolean networks. The ASP model is self-descriptive, i.e. it does not rely on any implicit assumptions or background knowledge, while with boolean networks, the user needs to check the conditions for every node before execution.

1.3 Network execution

We use the **clingo** Gebser et al. (2007) system that combines grounder and solver in one package to compute the answer sets. To compute the answer sets with incremental approach we use the extension of clingo, called **iclingo** Gebser et al. (2008).

In Tables 1 and 2 we provide the results for the Budding Yeast and Fission Yeast network trajectories from an initial state that corresponds to the point of cell division initiation. Each table is a structured representation of the derived answer set. Rows stand for proteins, and columns stand for the time flow, i.e. one row shows the changes of the protein over time. For brevity, we denote an *act*/2 state with 1 in the appropriate cell and *inh*/2 with 0. For example, *act*(*SK*, 0) converts to 1 in row SK and column 0, etc. These trajectories and the resulting stable states have also been found in Davidich & Bornholdt (2008) and Li et al. (2004). In fact all stable states obtained by the Fission Yeast network correspond to those reported in Davidich & Bornholdt (2008) and the ones obtained by the Budding Yeast network correspond to those reported in Li et al. (2004).

time	cln3	mbf	sbf	cln12	cdh1	swi5	cdc20	clb56	sic1	clb12	mcm1
1	1	0	0	0	1	0	0	0	1	0	0
2	0	1	1	0	1	0	0	0	1	0	0
3	0	1	1	1	1	0	0	0	1	0	0
4	0	1	1	1	0	0	0	0	0	0	0
5	0	1	1	1	0	0	0	1	0	0	0
6	0	1	1	1	0	0	0	1	0	1	1
7	0	0	0	1	0	0	1	1	0	1	1
8	0	0	0	0	0	1	1	0	0	1	1
9	0	0	0	0	0	1	1	0	1	1	1
10	0	0	0	0	0	1	1	0	1	0	1
11	0	0	0	0	1	1	1	0	1	0	0
12	0	0	0	0	1	1	0	0	1	0	0
13	0	0	0	0	1	0	0	0	1	0	0
14	0	0	0	0	1	0	0	0	1	0	0

Table 1: The Budding Yeast network execution flow

time	start	SK	cdc2	ste9	rum1	slp1	cdc2_*	wee1	cdc25	pp
1	1	0	0	1	1	0	0	1	0	0
2	0	1	0	1	1	0	0	1	0	0
3	0	0	0	0	0	0	0	1	0	0
4	0	0	1	0	0	0	0	1	0	0
5	0	0	1	0	0	0	0	0	1	0
6	0	0	1	0	0	0	1	0	1	0
7	0	0	1	0	0	1	1	0	1	0
8	0	0	0	0	0	1	0	0	1	1
9	0	0	0	1	1	0	0	1	0	1
10	0	0	0	1	1	0	0	1	0	0
11	0	0	0	1	1	0	0	1	0	0

Table 2: The Fission Yeast network execution flow

References

- Davidich, M. I. & Bornholdt, S. (2008), ‘Boolean network model predicts cell cycle sequence of fission yeast’, *PLoS ONE* **3**(2), e1672.
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