Supplementary Material

Comparing Boolean and piecewise affine differential models for genetic networks

Madalena Chaves, Laurent Tournier, and Jean-Luc Gouzé

1 Discrete (multi-level) and Boolean models

The example used in this paper is a piecewise affine (PWA) model of the nutritional stress response in *E. coli* developed by Ropers et al (2006) and analysed from the mathematical point of view by Grognard et al (2007) (the mathematical model is given in the main text).

Following the methods described in the main text, a multi-level discrete model and then a strictly Boolean model were constructed from the PWA system. To illustrate the construction of the transition tables corresponding to the multi-level and Boolean model we next give the complete tables (the full tables can also be found in Chaves et al (2009)).

Table 1 shows the multi-level model rules for *cya*, in the cases $U = 0$ or $U = 1$ (the two columns under U or Y^+ correspond to the cases $U = 0$ or $U = 1$). The columns C and Y contain the multi-level states corresponding to the (continuous) variables x_c and x_y, obtained by application of equation (3) in the main text. The column Y^+ shows the synchronous state transition, computed according to equation (4). Columns Y_1^+ and Y_2^+ of Table 1 represent the Boolean variables corresponding to Y^+, computed according to hypotheses H1 and H2.

Note that both discrete variables Y and C have 3 possible values so, according to hypotheses H1 and H2, each of them will give rise to two Boolean variables: Y_1, Y_2 and C_1, C_2. These are depicted in the first four columns of Table 2. The synchronous Boolean updates for the two *cya* logical variables are shown in the columns Y_1^+ and Y_2^+. As explained in the text, there are Boolean state combinations which have no biological meaning: these are the rows highlighted in grey and represent the forbidden states in $S_{D,f}$. The corresponding entries in columns Y_1^+ and Y_2^+ are filled following points 1 to 3, in Appendix 1 (main text). Therefore, according to Lemma 1, there are no transitions to forbidden states.

All the tables represent the synchronous updates for the discrete and Boolean models. To obtain an asynchronous trajectory, one allows only one of the variables to change at a time.

The transition tables for the other variables were similarly constructed. For the variables *crp* and *fis*, the rules were determined separately for $U = 0$ and $U = 1$. The expression H_i^0 (resp., H_i^1) denotes the Boolean rule for variable F_i when $U = 0$ (resp., U).

From the Tables, one can deduce the final updating rules for the Boolean model:

$$
\begin{aligned}
U^+ &= U \\
C_1^+ &= 1 \\
C_2^+ &= (\overline{U} \wedge C_1 \wedge \overline{F_1}) \vee (U \wedge C_1 \wedge \overline{F_2} \wedge \overline{F_3} \wedge \overline{F_4}) \\
Y_1^+ &= 1 \\
Y_2^+ &= (\overline{U} \wedge Y_1) \vee (U \wedge [(Y_1 \wedge (\overline{C_1} \vee \overline{C_2})) \vee ((Y_1 \wedge \overline{Y_2}) \wedge C_1 \wedge C_2)]) \\
G_1^+ &= (\overline{F_3} \wedge \overline{F_4}) \vee [(F_1 \wedge F_2 \wedge F_3) \vee G_2] \\
G_2^+ &= \overline{F_3} \wedge \overline{F_4} \wedge G_1 \wedge (\overline{G_2} \vee T_1 \vee T_2) \\
T_1^+ &= [\overline{F_3} \wedge \overline{F_4} \wedge T_2] \vee [F_1 \wedge F_2 \wedge F_3 \wedge ((\overline{G_2} \wedge T_2) \vee (G_2 \wedge (T_2 \vee \overline{T_1})))] \\
T_2^+ &= 0 \\
F_1^+ &= (\overline{U} \wedge H_1^0) \vee (U \wedge H_1^1) \\
F_2^+ &= (\overline{U} \wedge H_2^0) \vee (U \wedge H_2^1) \\
F_3^+ &= (\overline{U} \wedge H_3^0) \vee (U \wedge H_3^1) \\
F_4^+ &= (\overline{U} \wedge H_4^0) \vee (U \wedge H_4^1)
\end{aligned}
$$

where

$$
\begin{aligned}
H_1^0 &= 1 \\
H_2^0 &= (F_1 \wedge G_1 \wedge \overline{T_2}) \vee (F_1 \wedge F_2 \wedge F_3) \\
H_3^0 &= (F_1 \wedge F_2 \wedge G_1 \wedge \overline{T_2}) \vee (F_1 \wedge F_2 \wedge F_3 \wedge F_4) \\
H_4^0 &= (F_1 \wedge F_2 \wedge F_3 \wedge \overline{F_4} \wedge G_1 \wedge \overline{T_2}) \\
H_1^1 &= [((\overline{C_1} \wedge \overline{C_2}) \vee (\overline{Y_1} \wedge \overline{Y_2})) \wedge H_1^0] \vee [(C_1 \vee C_2 \vee Y_1 \vee Y_2) \wedge F_1 \wedge F_2] \\
H_2^1 &= [((\overline{C_1} \wedge \overline{C_2}) \vee (\overline{Y_1} \wedge \overline{Y_2})) \wedge H_2^0] \vee [(C_1 \vee C_2 \vee Y_1 \vee Y_2) \wedge F_1 \wedge F_2 \wedge F_3] \\
H_3^1 &= [((\overline{C_1} \wedge \overline{C_2}) \vee (\overline{Y_1} \wedge \overline{Y_2})) \wedge H_3^0] \vee [(C_1 \vee C_2 \vee Y_1 \vee Y_2) \wedge F_1 \wedge F_2 \wedge F_3 \wedge F_4] \\
H_4^1 &= [((\overline{C_1} \wedge \overline{C_2}) \vee (\overline{Y_1} \wedge \overline{Y_2})) \wedge H_4^0]
\end{aligned}
$$

References

Chaves M, Tournier L, Gouzé JL (2009) Comparison between boolean and piecewise affine differential models for genetic networks. Tech. Rep. RR-7070, INRIA, http://hal.inria.fr/inria-00426414/en/

Grognard F, Gouzé JL, de Jong H (2007) Piecewise-linear models of genetic regulatory networks: theory and example. In: Queinnec I, Tarbouriech S, Garcia G, Niculescu S (eds) Biology and control theory: current challenges, Lecture Notes in Control and Information Sciences (LNCIS) 357, Springer-Verlag, pp 137–159

Ropers D, de Jong H, Page M, Schneider D, Geiselmann J (2006) Qualitative simulation of the carbon starvation response in *Escherichia coli*. Biosystems 84(2):124–152

Table 1: Multi-level model for *cya* (Y).

C	Y	U	Y^+	Y_1^+	Y_2^+
0	0	0 1	1 1	1 1	0 0
0	1	0 1	2 2	1 1	1 1
0	2	0 1	2 2	1 1	1 1
1	0	0 1	1 1	1 1	0 0
1	1	0 1	2 2	1 1	1 1
1	2	0 1	2 2	1 1	1 1
2	0	0 1	1 1	1 1	0 0
2	1	0 1	2 2	1 1	1 1
2	2	0 1	2 1	1 1	1 0

Table 2: Boolean model for *cya*.

C_1	C_2	Y_1	Y_2	U	Y_1^+	Y_2^+
0	0	0	0	0 1	1 1	0 0
0	0	0	1	0 1	1 1	0 0
0	0	1	0	0 1	1 1	1 1
0	0	1	1	0 1	1 1	1 1
0	1	0	0	0 1	1 1	0 0
0	1	0	1	0 1	1 1	0 0
0	1	1	0	0 1	1 1	1 1
0	1	1	1	0 1	1 1	1 1
1	0	0	0	0 1	1 1	0 0
1	0	0	1	0 1	1 1	0 0
1	0	1	0	0 1	1 1	1 1
1	0	1	1	0 1	1 1	1 1
1	1	0	0	0 1	1 1	0 0
1	1	0	1	0 1	1 1	0 0
1	1	1	0	0 1	1 1	1 1
1	1	1	1	0 1	1 1	1 0

Table 3: Multi-level and Boolean models for *crp* (C), case $U = 1$.

C_1	C_2	Y_1	Y_2	C	Y	F		C^+		C_1^+		C_2^+	
0	0	0	0	0	0	< 2	≥ 2	1	1	1	1	0	0
0	0	0	1	-	-	-	-	-	-	1	1	0	0
0	0	1	0	0	1	< 2	≥ 2	1	1	1	1	0	0
0	0	1	1	0	2	< 2	≥ 2	1	1	1	1	0	0
0	1	0	0	-	-	-	-	-	-	1	1	0	0
0	1	0	1	-	-	-	-	-	-	1	1	0	0
0	1	1	0	-	-	-	-	-	-	1	1	0	0
0	1	1	1	-	-	-	-	-	-	1	1	0	0
1	0	0	0	1	0	< 2	≥ 2	2	1	1	1	1	0
1	0	0	1	-	-	-	-	-	-	1	1	1	0
1	0	1	0	1	1	< 2	≥ 2	2	1	1	1	1	0
1	0	1	1	1	2	< 2	≥ 2	2	1	1	1	1	0
1	1	0	0	2	0	< 2	≥ 2	2	1	1	1	1	0
1	1	0	1	-	-	-	-	-	-	1	1	1	0
1	1	1	0	2	1	< 2	≥ 2	2	1	1	1	1	0
1	1	1	1	2	2	< 2	≥ 2	2	1	1	1	1	0

Table 4: Multi-level and Boolean models for *crp*, case $U = 0$.

C_1	C_2	C	F	C^+	C_1^+	C_2^+
0	0	0	0	1	1	0
0	0	0	≥ 1	1	1	0
0	1	-	0	-	1	0
0	1	-	≥ 1	-	1	0
1	0	1	0	2	1	1
1	0	1	≥ 1	1	1	0
1	1	2	0	2	1	1
1	1	2	≥ 1	1	1	0

Table 5: Multi-level model for *gyrAB* (G) and *topA* (T).

G	T	F	G^+	T^+	G_1^+	G_2^+	T_1^+	T_2^+
0	0	<3 ≥ 3	1 0	0 0	1 0	0 0	0 0	0 0
0	1	<3 ≥ 3	1 0	0 0	1 0	0 0	0 0	0 0
0	2	<3 ≥ 3	1 0	1 1	1 0	0 0	1 1	0 0
1	0	<3 ≥ 3	2 0	0 0	1 0	1 0	0 0	0 0
1	1	<3 ≥ 3	2 0	0 0	1 0	1 0	0 0	0 0
1	2	<3 ≥ 3	2 0	1 1	1 0	1 0	1 1	0 0
2	0	<3 ≥ 3	1 1	0 1	1 1	0 0	0 1	0 0
2	1	<3 ≥ 3	2 1	0 0	1 1	1 0	0 0	0 0
2	2	<3 ≥ 3	2 1	1 1	1 1	1 0	1 1	0 0

Table 6: Boolean model for *gyrAB* and *topA*.

G_1	G_2	T_1	T_2	F	G_1^+	G_2^+	T_1^+	T_2^+
0	0	0	0	<3 ≥ 3	1 0	0 0	0 0	0 0
0	0	0	1	<3 ≥ 3	1 0	0 0	1 1	0 0
0	0	1	0	<3 ≥ 3	1 0	0 0	0 0	0 0
0	0	1	1	<3 ≥ 3	1 0	0 0	1 1	0 0
0	1	0	0	<3 ≥ 3	1 1	0 0	0 1	0 0
0	1	0	1	<3 ≥ 3	1 1	0 0	1 1	0 0
0	1	1	0	<3 ≥ 3	1 1	0 0	0 0	0 0
0	1	1	1	<3 ≥ 3	1 1	0 0	1 1	0 0
1	0	0	0	<3 ≥ 3	1 0	1 0	0 0	0 0
1	0	0	1	<3 ≥ 3	1 0	1 0	1 1	0 0
1	0	1	0	<3 ≥ 3	1 0	1 0	0 0	0 0
1	0	1	1	<3 ≥ 3	1 0	1 0	1 1	0 0
1	1	0	0	<3 ≥ 3	1 1	0 0	0 1	0 0
1	1	0	1	<3 ≥ 3	1 1	1 0	1 1	0 0
1	1	1	0	<3 ≥ 3	1 1	1 0	0 0	0 0
1	1	1	1	<3 ≥ 3	1 1	1 0	1 1	0 0

Table 7: Multi-level model for *fis* (F), case $U = 0$.

G	T	F	F^+
0	0	0 1 2 3 4	1 1 1 2 3
0	1	0 1 2 3 4	1 1 1 2 3
0	2	0 1 2 3 4	1 1 1 2 3
1	0	0 1 2 3 4	1 2 3 4 3
1	1	0 1 2 3 4	1 2 3 4 3
1	2	0 1 2 3 4	1 1 1 2 3
2	0	0 1 2 3 4	1 2 3 4 3
2	1	0 1 2 3 4	1 2 3 4 3
2	2	0 1 2 3 4	1 1 1 2 3

Table 8: Boolean model for *fis*, case $U = 0$.

G_1	G_2	T_1	T_2	F	F_1^+	F_2^+	F_3^+	F_4^+
0	0	0	0	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	0	0	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	0	1	0	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	0	1	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	1	0	0	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	1	0	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	1	1	0	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	1	1	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	0	0	0	0 1 2 3 4	1 1 1 1 1	0 1 1 1 1	0 0 1 1 1	0 0 0 1 0
1	0	0	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	0	1	0	0 1 2 3 4	1 1 1 1 1	0 1 1 1 1	0 0 1 1 1	0 0 0 1 0
1	0	1	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	1	0	0	0 1 2 3 4	1 1 1 1 1	0 1 1 1 1	0 0 1 1 1	0 0 0 1 0
1	1	0	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	1	1	0	0 1 2 3 4	1 1 1 1 1	0 1 1 1 1	0 0 1 1 1	0 0 0 1 0
1	1	1	1	0 1 2 3 4	1 1 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0

Table 9: Multi-level model for *fis*, case $U = 1$ and $C = 0$ or $Y = 0$.

C	Y	G	T	F	F^+
		0	0	0 1 2 3 4	1 1 1 2 3
		0	1	0 1 2 3 4	1 1 1 2 3
		0	2	0 1 2 3 4	1 1 1 2 3
0	*	1	0	0 1 2 3 4	1 2 3 4 3
		1	1	0 1 2 3 4	1 2 3 4 3
*	0	1	2	0 1 2 3 4	1 1 1 2 3
		2	0	0 1 2 3 4	1 2 3 4 3
		2	1	0 1 2 3 4	1 2 3 4 3
		2	2	0 1 2 3 4	1 1 1 2 3
1,2	1,2	*	*	0 1 2 3 4	0 0 1 2 3

Table 10: Boolean model for *fis*, case $U = 1$, and $C, Y \in \{1, 2\}$.

C_1	C_2	Y_1	Y_2	F	F_1^+	F_2^+	F_3^+	F_4^+
0	1	0	1	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	1	1	0	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
0	1	1	1	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	0	0	1	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	0	1	0	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	0	1	1	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	1	0	1	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	1	1	0	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0
1	1	1	1	0 1 2 3 4	0 0 1 1 1	0 0 0 1 1	0 0 0 0 1	0 0 0 0 0