Biodivne Boolean Models: A Comprehensive Logical Modelling Benchmark

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Abstract

Recent years have seen emergence of a wide variety of powerful tools for computational analysis of logical models represented as Boolean networks. However, assessment of validity, efficiency and scalability of such tools requires a comprehensive benchmark set of Boolean networks that can be used to obtain comparable results for different tools.

At the moment, this need is largely served using databases of biological models such as CellCollective or GINsim database. However, these databases are more focused on human curated, biological aspects of the networks and are therefore limited in scope. Furthermore, the models in these databases are not available as a single dataset and often have to be manually obtained one by one.

Here, we introduce a comprehensive benchmark dataset that has been created by surveying the aforementioned databases, as well as a large body of other literature to obtain as many biologically motivated Boolean networks as possible. To make the dataset useful to a wide range of tool maintainers, we provide the models in different machine-readable formats and ensure all models are valid and consistent using an automated validation procedure. At the moment, the dataset comprises 145 networks.

1 Introduction

Logical models provide a very useful and simple framework for description of complex biological processes. The most common mechanism for describing executable logical models are Boolean networks. In recent years, we have seen a rapid development of new tools and algorithms for analysis of large Boolean networks. However, in many instances, it is hard to assess usefulness and scalability of such tools due to a lack of commonly recognised "benchmark dataset" of networks on which the tools can be compared.

This purpose is often served by models obtained from databases maintained by the authors of some of the larger modelling tools, such as CellCollective [29] or GINsim [53]. However, these models are often hard to obtain in bulk and have to be downloaded one by one. Additionally, authors often modify the models slightly, or assume non-standard values of inputs which prevents comparisons. Finally, these databases are far from comprehensive, so a wide range of models is often omitted.

As a result, most papers develop an ad hoc benchmark set that is often partially proprietary and hard or impossible to replicate and compare to. Here, we propose a standardized comprehensive benchmark set that can be used for this purpose instead. To make the benchmark set as user friendly as possible, we provide the following benefits compared to existing solutions:

- The dataset is open source and available on Github, so that anyone can propose new additions or modifications. Each tracked model is (primarily) referred to using a unique ID as opposed to name or citation. However, we also keep track of the original source (publication) where the model first appeared.
- Every model is provided in three formats that can be consumed by different tools or easily parsed by a new tool. Namely, we consider `bnet`, as popularised by PyBoolNet [37], `aeon` format as used in AEON [4], and the universal SBML-qual [7] format.
- If the model contains inputs (constants), aside from the model as published by the authors, we also generate two variants with all inputs fixed to `true` and `false`, and a variant where the values of all inputs are unspecified.
- For each model format and variant, we provide a single bundle with all available models that can be easily used for batch processing.
- We provide an automated procedure to check the validity and integrity of all included models, as well as generate different model bundles. This minimises possible user errors when adding new models.

This document then serves as a cumulative report of all the models included in the dataset and the sources of these models.

2 Models

ID	Name	Vars.	Inps.	Regs.	Source
001	SIGNALING IN MACROPHAGE ACTIVATION	302	19	533	[59, 29]
002	SIGNAL TRANSDUCTION IN FIBROBLASTS	130	9	557	[28, 29]
003	MAMMALIAN CELL CYCLE	19	1	51	[67, 29]
004	ERBB RECEPTOR SIGNALING	225	22	1100	[27, 29]
005	FA/BRCA PATHWAY	28	0	123	[61, 29]
006	HGF SIGNALING IN KERATINOCYTES	62	6	103	[71, 29]
007	CORTICAL AREA DEVELOPMENT	5	0	14	[22, 29]
008	DEATH RECEPTOR SIGNALING	25	3	45	[6, 29]
009	YEAST APOPTOSIS	60	13	114	[34, 29]
010	CARDIAC-DEVELOPMENT	13	2	37	[30, 29]
011	GUARD CELL ABSCISIC ACID SIGNALING	40	4	78	[39, 29]
012	T-CELL RECEPTOR SIGNALING	94	7	158	[66, 29]
013	CHOLESTEROL REGULATORY PATHWAY	32	2	41	[35, 29]
014	T-LGL SURVIVAL NETWORK 2008	54	7	193	[78, 29]
015	NEUROTRANSMITTER SIGNALING PATHWAY	14	2	20	[26, 29]
016	IL-1 SIGNALING	104	14	218	[64, 29]
017	DIFFERENTIATION OF T-LYMPHOCYTES	41	9	97	[45, 29]
018	EGFR-ERBB SIGNALING	76	28	226	[68, 29]
019	IL-6 SIGNALING	71	15	149	[64, 29]
020	APOPTOSIS NETWORK	39	2	73	[42, 29]
021	BODY SEGMENTATION IN DROSOPHILA 2013	14	3	29	[43, 29]
022	B-CELL DIFFERENTIATION	17	5	39	[47, 29]
023	MAMMALIAN CELL CYCLE 2006	9	1	34	[19, 29]
024	BUDDING YEAST CELL CYCLE	16	4	42	[75, 29]
025	T-LGL SURVIVAL NETWORK 2011	54	6	195	[65, 29]
026	BUDDING YEAST CELL CYCLE 2009	18	0	59	[31, 29]
027	WG PATHWAY OF DROSOPHILA	12	14	29	[46, 29]
028	VEGF PATHWAY OF DROSOPHILA	10	8	18	[46, 29]
029	TOLL PATHWAY OF DROSOPHILA	9	2	11	[46, 29]
030	SPZ NETWORK OF DROSOPHILA	18	6	28	[46, 29]

ID	Name	Vars.	Inps.	Regs.	Source
031	CELL CYCLE TRANSCRIPTION	9	0	19	[55, 29]
032	T-CELL SIGNALLING 2006	37	3	53	[36, 29]
033	BT474 BREAST CELL LINE LONG TERM	19	5	68	[17, 29]
034	HCC1954 BREAST CELL LINE LONG TERM	19	4	68	[17, 29]
035	BT474 BREAST CELL LINE SHORT TERM	11	5	46	[17, 29]
036	HCC1954 BREAST CELL LINE SHORT TERM	11	5	46	[17, 29]
037	SKBR3 BREAST CELL LINE SHORT TERM	11	5	41	[17, 29]
038	SKBR3 BREAST CELL LINE LONG TERM	21	4	81	[17, 29]
039	HIV-1 INTERACTIONS WITH T-CELL SIGNALING	124	14	368	[58, 29]
040	T-CELL DIFFERENTIATION	19	4	34	[49, 29]
041	INFLUENZA VIRUS REPLICATION CYCLE	120	11	302	[41, 29]
042	TOL REGULATORY NETWORK	14	10	48	[70, 29]
043	BORDETELLA BRONCHISEPTICA	33	0	79	[74, 29]
044	TRICHOSTRONGYLUS RETORTAEFORMIS	25	1	58	[74, 29]
045	HH PATHWAY OF DROSOPHILA	11	13	32	[46, 29]
046	B BRONCHISEPTICA AND T RETORTAEFORMIS	52	1	135	[74, 29]
047	FGF PATHWAY OF DROSOPHILA	14	9	24	[46, 29]
048	GLUCOSE REPRESSION SIGNALING 2009	55	18	97	[9, 29]
049	OXIDATIVE STRESS PATHWAY	18	1	32	[72, 29]
050	CD4 T-CELL SIGNALING	154	34	351	[13, 29]
051	COLITIS ASSOCIATED COLON CANCER	69	1	153	[40, 29]
052	SEPTATION INITIATION NETWORK	23	8	50	[8, 29]
053	PREDICTING VARIABILITIES IN CARDIAC GENE	13	2	37	[24, 29]
054	PC12 CELL DIFFERENTIATION	61	1	108	[54, 29]
055	HUMAN GONADAL SEX DETERMINATION	19	0	79	[60, 29]
056	IGVH MUTATIONS IN LYMPHOCYTIC LEUKEMIA	66	25	125	[1, 29]

ID	Name	Vars.	Inps.	Regs.	Source
057	FANCONI ANEMIA AND CHECKPOINT RECOVERY	15	0	66	[62, 29]
058	ARABIDOPSIS THALIANA CELL CYCLE	14	0	66	[56, 29]
059	BORTEZOMIB RESPONSES IN MYELOMA CELLS	62	5	131	[10, 29]
060	STOMATAL OPENING	44	5	167	[21, 29]
061	TUMOR MICROENVIRONMENT IN LYMPHOBLASTIC LEUKAEMIA	24	2	79	[18, 29]
062	CD4 T-CELL DIFFERENTIATION AND PLASTICITY	12	6	78	[44, 29]
063	LAC OPERON	10	3	22	[76, 29]
064	METABOLIC INTERACTIONS IN GUT MICROBIOME	8	4	27	[73, 29]
065	TUMOUR CELL INVASION AND MIGRATION	30	2	156	[11, 29]
066	CD4 T-CELL DIFFERENTIATION	29	9	96	[29]
067	REGULATION OF L-ARABINOSE OPERON	9	4	18	[33, 29]
068	AURORA KINASE-A IN NEUROBLASTOMA	19	4	43	[15, 29]
069	IRON ACQUISITION AND STRESS RESPONSE	20	2	38	[5, 29]
070	MAPK CANCER CELL FATE	49	4	104	[25, 29]
071	CASTRATION RESISTANT PROSTATE CANCER	28	14	51	[2, 29]
072	LYMPHOPOIESIS REGULATORY NETWORK	67	14	160	[48, 29]
073	LYMPHOID AND MYELOID CELL SPECIFICATION	31	2	94	[12, 29]
074	T-LGL SURVIVAL NETWORK 2011 REDUCED	18	0	43	[65, 29]
075	INFLAMMATORY BOWEL DISEASE	47	0	287	[3, 29]
076	SENESCENCE ASSOCIATED SECRETORY PHENOTYPE	49	2	96	[50, 29]
077	SIGNALLING PATHWAY FOR BUTANOL PRODUCTION	53	13	139	[52, 29]
078	IMMUNE SYSTEM	151	13	506	[29]
079	----	–	–	–	–
080	TCR SIGNALING 2018	95	15	212	[63, 53]
081	TLR5 SIGNALING 2018	40	2	68	[63, 53]
082	TCR-TLR5 SIGNALING 2018	112	16	257	[63, 53]
083	SIGNALING IN PROSTATE CANCER	122	11	420	[51, 53]
084	----	–	–	–	–
085	----	–	–	–	–

ID	Name	Vars.	Inps.	Regs.	Source
086	TUMOUR CELL INVASION AND MIGRATION REDUCED	18	2	88	[11, 53]
087	----	–	–	–	–
088	MIR-9 NEUROGENESIS	6	0	11	[14, 53]
089	MAPK REDUCED 1	13	4	78	[25, 53]
090	MAPK REDUCED 2	14	4	60	[25, 53]
091	MAPK REDUCED 3	12	4	58	[25, 53]
092	----	–	–	–	–
093	IMMUNE CHECKPOINT INHIBITORS	51	15	128	[38, 53]
094	----	–	–	–	–
095	FISSION YEAST 2008	9	1	27	[16, 53]
096	ERBB REGULATED G1-S TRANSITION	19	1	48	[32, 53]
097	DROSOPHILA WINGS AP	8	2	14	[23, 53]
098	----	–	–	–	–
099	----	–	–	–	–
100	----	–	–	–	–
101	----	–	–	–	–
102	----	–	–	–	–
103	----	–	–	–	–
104	DROSOPHILA CELL CYCLE	11	3	42	[20, 53]
105	----	–	–	–	–
106	----	–	–	–	–
107	----	–	–	–	–
108	GEROCONVERSION	23	2	67	[77, 53]
109	ASYMMETRIC CELL DIVISION A	5	0	15	[69, 53]
110	ASYMMETRIC CELL DIVISION B	9	0	12	[69, 53]
111	APOPTOSIS	18	15	40	[57]
112	COAGULATION PATHWAY	85	27	195	[57]
113	ER STRESS	107	75	266	[57]
114	ETC	46	38	154	[57]
115	E PROTEIN	17	18	40	[57]
116	HMOX1 PATHWAY	89	55	228	[57]
117	IFN LAMBDA	28	19	52	[57]
118	INTERFERON 1	66	55	190	[57]
119	JNK PATHWAY	13	6	21	[57]
120	KYNURENINE PATHWAY	78	72	304	[57]
121	NLRP3 ACTIVATION	39	18	91	[57]
122	NSP14	74	94	558	[57]
123	NSP4 NSP6	43	17	62	[57]
124	NSP9 PROTEIN	119	133	257	[57]
125	ORF10 CUL2 PATHWAY	34	17	92	[57]

ID	Name	Vars.	Inps.	Regs.	Source
126	`ORF3A`	24	18	56	[57]
127	`PAMP SIGNALING`	44	35	109	[57]
128	`PYRIMIDINE DEPRIVATION`	56	34	131	[57]
129	`RTC AND TRANSCRIPTION`	33	1	40	[57]
130	`RENIN ANGIOTENSIN`	43	34	130	[57]
131	`TGFB PATHWAY`	7	14	24	[57]
132	`VIRUS REPLICATION CYCLE`	129	19	268	[57]

References

[1] María Camila Álvarez-Silva, Sally Yepes, Maria Mercedes Torres, and Andres Fernando Gonzalez Barrios. Proteins interaction network and modeling of igvh mutational status in chronic lymphocytic leukemia. *Theoretical Biology and Medical Modelling*, 12(1):1–15, 2015.

[2] Osama Ali Arshad and Aniruddha Datta. Towards targeted combinatorial therapy design for the treatment of castration-resistant prostate cancer. *BMC bioinformatics*, 18(4):5–15, 2017.

[3] Violeta Balbas-Martinez, Leire Ruiz-Cerdá, Itziar Irurzun-Arana, Ignacio González-García, An Vermeulen, José David Gómez-Mantilla, and Iñaki F Trocóniz. A systems pharmacology model for inflammatory bowel disease. *PloS one*, 13(3):e0192949, 2018.

[4] Nikola Beneš, Luboš Brim, Jakub Kadlecaj, Samuel Pastva, and David Šafránek. AEON: attractor bifurcation analysis of parametrised boolean networks. In *International Conference on Computer Aided Verification*, pages 569–581. Springer, 2020.

[5] Madison Brandon, Brad Howard, Christopher Lawrence, and Reinhard Laubenbacher. Iron acquisition and oxidative stress response in aspergillus fumigatus. *BMC systems biology*, 9(1):1–18, 2015.

[6] Laurence Calzone, Laurent Tournier, Simon Fourquet, Denis Thieffry, Boris Zhivotovsky, Emmanuel Barillot, and Andrei Zinovyev. Mathematical modelling of cell-fate decision in response to death receptor engagement. *PLoS Comput Biol*, 6(3):e1000702, 2010.

[7] Claudine Chaouiya, Duncan Bérenguier, Sarah M Keating, Aurélien Naldi, Martijn P Van Iersel, Nicolas Rodriguez, Andreas Dräger, Finja Büchel, Thomas Cokelaer, Bryan Kowal, et al. Sbml qualitative models: a model representation format and infrastructure to foster interactions between qualitative modelling formalisms and tools. *BMC systems biology*, 7(1):1–15, 2013.

[8] Anastasia Chasapi, Paulina Wachowicz, Anne Niknejad, Philippe Collin, Andrea Krapp, Elena Cano, Viesturs Simanis, and Ioannis Xenarios. An

extended, boolean model of the septation initiation network in s. pombe provides insights into its regulation. *PloS one*, 10(8):e0134214, 2015.

[9] Tobias S Christensen, Ana Paula Oliveira, and Jens Nielsen. Reconstruction and logical modeling of glucose repression signaling pathways in saccharomyces cerevisiae. *BMC systems biology*, 3(1):1–15, 2009.

[10] Vaishali L Chudasama, Meric A Ovacik, Darrell R Abernethy, and Donald E Mager. Logic-based and cellular pharmacodynamic modeling of bortezomib responses in u266 human myeloma cells. *Journal of Pharmacology and Experimental Therapeutics*, 354(3):448–458, 2015.

[11] David PA Cohen, Loredana Martignetti, Sylvie Robine, Emmanuel Barillot, Andrei Zinovyev, and Laurence Calzone. Mathematical modelling of molecular pathways enabling tumour cell invasion and migration. *PLoS computational biology*, 11(11):e1004571, 2015.

[12] Samuel Collombet, Chris van Oevelen, Jose Luis Sardina Ortega, Wassim Abou-Jaoudé, Bruno Di Stefano, Morgane Thomas-Chollier, Thomas Graf, and Denis Thieffry. Logical modeling of lymphoid and myeloid cell specification and transdifferentiation. *Proceedings of the National Academy of Sciences*, 114(23):5792–5799, 2017.

[13] Brittany D Conroy, Tyler A Herek, Timothy D Shew, Matthew Latner, Joshua J Larson, Laura Allen, Paul H Davis, Tomáš Helikar, and Christine E Cutucache. Design, assessment, and in vivo evaluation of a computational model illustrating the role of cav1 in cd4+ t-lymphocytes. *Frontiers in immunology*, 5:599, 2014.

[14] Marion Coolen, Denis Thieffry, Øyvind Drivenes, Thomas S Becker, and Laure Bally-Cuif. mir-9 controls the timing of neurogenesis through the direct inhibition of antagonistic factors. *Developmental cell*, 22(5):1052–1064, 2012.

[15] Meike Dahlhaus, Andre Burkovski, Falk Hertwig, Christoph Mussel, Ruth Volland, Matthias Fischer, Klaus-Michael Debatin, Hans A Kestler, and Christian Beltinger. Boolean modeling identifies greatwall/mastl as an important regulator in the aurka network of neuroblastoma. *Cancer letters*, 371(1):79–89, 2016.

[16] Maria I Davidich and Stefan Bornholdt. Boolean network model predicts cell cycle sequence of fission yeast. *PloS one*, 3(2):e1672, 2008.

[17] Silvia Von der Heyde, Christian Bender, Frauke Henjes, Johanna Sonntag, Ulrike Korf, and Tim Beissbarth. Boolean ErbB network reconstructions and perturbation simulations reveal individual drug response in different breast cancer cell lines. *BMC systems biology*, 8(1):1–22, 2014.

[18] Jennifer Enciso, Hector Mayani, Luis Mendoza, and Rosana Pelayo. Modeling the pro-inflammatory tumor microenvironment in acute lymphoblastic leukemia predicts a breakdown of hematopoietic-mesenchymal communication networks. *Frontiers in physiology*, 7:349, 2016.

[19] Adrien Fauré, Aurélien Naldi, Claudine Chaouiya, and Denis Thieffry. Dynamical analysis of a generic Boolean model for the control of the mammalian cell cycle. *Bioinformatics*, 22(14):e124–e131, 2006.

[20] Adrien Fauré and Denis Thieffry. Logical modelling of cell cycle control in eukaryotes: a comparative study. *Molecular BioSystems*, 5(12):1569–1581, 2009.

[21] Xiao Gan and Réka Albert. Analysis of a dynamic model of guard cell signaling reveals the stability of signal propagation. *BMC systems biology*, 10(1):1–14, 2016.

[22] Clare E Giacomantonio and Geoffrey J Goodhill. A boolean model of the gene regulatory network underlying mammalian cortical area development. *PLoS Comput Biol*, 6(9):e1000936, 2010.

[23] Aitor González, Claudine Chaouiya, and Denis Thieffry. Dynamical analysis of the regulatory network defining the dorsal–ventral boundary of the drosophila wing imaginal disc. *Genetics*, 174(3):1625–1634, 2006.

[24] Melanie Grieb, Andre Burkovski, J Eric Sträng, Johann M Kraus, Alexander Groß, Günther Palm, Michael Kühl, and Hans A Kestler. Predicting variabilities in cardiac gene expression with a boolean network incorporating uncertainty. *PLoS One*, 10(7):e0131832, 2015.

[25] Luca Grieco, Laurence Calzone, Isabelle Bernard-Pierrot, François Radvanyi, Brigitte Kahn-Perles, and Denis Thieffry. Integrative modelling of the influence of mapk network on cancer cell fate decision. *PLoS computational biology*, 9(10):e1003286, 2013.

[26] Simone Gupta, Siddharth S Bisht, Ritushree Kukreti, Sanjeev Jain, and Samir K Brahmachari. Boolean network analysis of a neurotransmitter signaling pathway. *Journal of theoretical biology*, 244(3):463–469, 2007.

[27] Tomáš Helikar, Naomi Kochi, Bryan Kowal, Manjari Dimri, Mayumi Naramura, Srikumar M Raja, Vimla Band, Hamid Band, and Jim A Rogers. A comprehensive, multi-scale dynamical model of erbb receptor signal transduction in human mammary epithelial cells. *PloS one*, 8(4):e61757, 2013.

[28] Tomáš Helikar, John Konvalina, Jack Heidel, and Jim A Rogers. Emergent decision-making in biological signal transduction networks. *Proceedings of the National Academy of Sciences*, 105(6):1913–1918, 2008.

[29] Tomáš Helikar, Bryan Kowal, Sean McClenathan, Mitchell Bruckner, Thaine Rowley, Alex Madrahimov, Ben Wicks, Manish Shrestha, Kahani Limbu, and Jim A Rogers. The cell collective: toward an open and collaborative approach to systems biology. *BMC systems biology*, 6(1):1–14, 2012.

[30] Franziska Herrmann, Alexander Groß, Dao Zhou, Hans A Kestler, and Michael Kühl. A boolean model of the cardiac gene regulatory network determining first and second heart field identity. *PloS one*, 7(10):e46798, 2012.

[31] David J Irons. Logical analysis of the budding yeast cell cycle. *Journal of theoretical biology*, 257(4):543–559, 2009.

[32] Nobuhisa Ito, Go Kuwahara, Yuta Sukehiro, and Hiromitsu Teratani. Segmental arterial mediolysis accompanied by renal infarction and pancreatic enlargement: a case report. *Journal of Medical Case Reports*, 6(1):1–5, 2012.

[33] Andy Jenkins and Matthew Macauley. Bistability and asynchrony in a boolean model of the l-arabinose operon in escherichia coli. *Bulletin of mathematical biology*, 79(8):1778–1795, 2017.

[34] Laleh Kazemzadeh, Marija Cvijovic, and Dina Petranovic. Boolean model of yeast apoptosis as a tool to study yeast and human apoptotic regulations. *Frontiers in physiology*, 3:446, 2012.

[35] Gwenael Kervizic and Laurent Corcos. Dynamical modeling of the cholesterol regulatory pathway with boolean networks. *BMC systems biology*, 2(1):1–14, 2008.

[36] Steffen Klamt, Julio Saez-Rodriguez, Jonathan A Lindquist, Luca Simeoni, and Ernst D Gilles. A methodology for the structural and functional analysis of signaling and regulatory networks. *BMC bioinformatics*, 7(1):1–26, 2006.

[37] Hannes Klarner, Adam Streck, and Heike Siebert. PyBoolNet: a python package for the generation, analysis and visualization of boolean networks. *Bioinformatics*, 33(5):770–772, 2017.

[38] Maria Kondratova, Emmanuel Barillot, Andrei Zinovyev, and Laurence Calzone. Modelling of immune checkpoint network explains synergistic effects of combined immune checkpoint inhibitor therapy and the impact of cytokines in patient response. *Cancers*, 12(12):3600, 2020.

[39] Song Li, Sarah M Assmann, and Réka Albert. Predicting essential components of signal transduction networks: a dynamic model of guard cell abscisic acid signaling. *PLoS Biol*, 4(10):e312, 2006.

[40] Junyan Lu, Hanlin Zeng, Zhongjie Liang, Limin Chen, Liyi Zhang, Hao Zhang, Hong Liu, Hualiang Jiang, Bairong Shen, Ming Huang, et al. Network modelling reveals the mechanism underlying colitis-associated colon cancer and identifies novel combinatorial anti-cancer targets. *Scientific reports*, 5(1):1–15, 2015.

[41] Alex Madrahimov, Tomáš Helikar, Bryan Kowal, Guoqing Lu, and Jim Rogers. Dynamics of influenza virus and human host interactions during infection and replication cycle. *Bulletin of mathematical biology*, 75(6):988–1011, 2013.

[42] Zhongxing Mai and Haiyan Liu. Boolean network-based analysis of the apoptosis network: irreversible apoptosis and stable surviving. *Journal of theoretical biology*, 259(4):760–769, 2009.

[43] Manuel Marques-Pita and Luis M Rocha. Canalization and control in automata networks: body segmentation in drosophila melanogaster. *PloS one*, 8(3):e55946, 2013.

[44] Mariana Esther Martinez-Sanchez, Luis Mendoza, Carlos Villarreal, and Elena R Alvarez-Buylla. A minimal regulatory network of extrinsic and intrinsic factors recovers observed patterns of cd4+ t cell differentiation and plasticity. *PLoS computational biology*, 11(6):e1004324, 2015.

[45] Pablo Martínez-Sosa and Luis Mendoza. The regulatory network that controls the differentiation of T lymphocytes. *Biosystems*, 113(2):96–103, 2013.

[46] Abibatou Mbodj, Guillaume Junion, Christine Brun, Eileen EM Furlong, and Denis Thieffry. Logical modelling of drosophila signalling pathways. *Molecular BioSystems*, 9(9):2248–2258, 2013.

[47] Akram Méndez and Luis Mendoza. A network model to describe the terminal differentiation of b cells. *PLoS computational biology*, 12(1):e1004696, 2016.

[48] Luis Mendoza and Akram Méndez. A dynamical model of the regulatory network controlling lymphopoiesis. *Biosystems*, 137:26–33, 2015.

[49] Luis Mendoza and Ioannis Xenarios. A method for the generation of standardized qualitative dynamical systems of regulatory networks. *Theoretical Biology and Medical Modelling*, 3(1):1–18, 2006.

[50] Patrick Meyer, Pallab Maity, Andre Burkovski, Julian Schwab, Christoph Müssel, Karmveer Singh, Filipa F Ferreira, Linda Krug, Harald J Maier, Meinhard Wlaschek, et al. A model of the onset of the senescence associated secretory phenotype after dna damage induced senescence. *PLoS computational biology*, 13(12):e1005741, 2017.

[51] Arnau Montagud, Jonas Béal, Luis Tobalina, Pauline Traynard, Vigneshwari Subramanian, Bence Szalai, Róbert Alföldi, László Puskás, Alfonso Valencia, Emmanuel Barillot, et al. Patient-specific boolean models of signalling networks guide personalised treatments. *Elife*, 11:e72626, 2022.

[52] Jana Musilová. Signaling pathway for butanol production in solventogenic clostridium bacteria. Master's thesis, Brno University of Technology, 2019.

[53] Aurélien Naldi, Céline Hernandez, Wassim Abou-Jaoudé, Pedro T Monteiro, Claudine Chaouiya, and Denis Thieffry. Logical modeling and analysis of cellular regulatory networks with ginsim 3.0. *Frontiers in physiology*, 9:646, 2018.

[54] Barbara Offermann, Steffen Knauer, Amit Singh, María L Fernández-Cachón, Martin Klose, Silke Kowar, Hauke Busch, and Melanie Boerries. Boolean modeling reveals the necessity of transcriptional regulation for bistability in pc12 cell differentiation. *Frontiers in genetics*, page 44, 2016.

[55] David A Orlando, Charles Y Lin, Allister Bernard, Jean Y Wang, Joshua ES Socolar, Edwin S Iversen, Alexander J Hartemink, and Steven B Haase. Global control of cell-cycle transcription by coupled cdk and network oscillators. *Nature*, 453(7197):944–947, 2008.

[56] Elizabeth Ortiz-Gutiérrez, Karla García-Cruz, Eugenio Azpeitia, Aaron Castillo, María de la Paz Sánchez, and Elena R Álvarez-Buylla. A dynamic gene regulatory network model that recovers the cyclic behavior of arabidopsis thaliana cell cycle. *PLoS computational biology*, 11(9):e1004486, 2015.

[57] Marek Ostaszewski, Alexander Mazein, Marc E Gillespie, Inna Kuperstein, Anna Niarakis, Henning Hermjakob, Alexander R Pico, Egon L Willighagen, Chris T Evelo, Jan Hasenauer, et al. Covid-19 disease map, building a computational repository of sars-cov-2 virus-host interaction mechanisms. *Scientific data*, 7(1):1–4, 2020.

[58] Oyebode J Oyeyemi, Oluwafemi Davies, David L Robertson, and Jean-Marc Schwartz. A logical model of hiv-1 interactions with the t-cell activation signalling pathway. *Bioinformatics*, 31(7):1075–1083, 2015.

[59] Sobia Raza, Kevin A Robertson, Paul A Lacaze, David Page, Anton J Enright, Peter Ghazal, and Tom C Freeman. A logic-based diagram of signalling pathways central to macrophage activation. *BMC systems biology*, 2(1):1–15, 2008.

[60] Osiris Ríos, Sara Frias, Alfredo Rodríguez, Susana Kofman, Horacio Merchant, Leda Torres, and Luis Mendoza. A boolean network model of human gonadal sex determination. *Theoretical Biology and Medical Modelling*, 12(1):1–18, 2015.

[61] Alfredo Rodriguez, David Sosa, Leda Torres, Bertha Molina, Sara Frias, and Luis Mendoza. A boolean network model of the fa/brca pathway. *Bioinformatics*, 28(6):858–866, 2012.

[62] Alfredo Rodríguez, Leda Torres, Ulises Juárez, David Sosa, Eugenio Azpeitia, Benilde García-de Teresa, Edith Cortés, Rocío Ortíz, Ana M Salazar, Patricia Ostrosky-Wegman, et al. Fanconi anemia cells with unrepaired dna damage activate components of the checkpoint recovery process. *Theoretical Biology and Medical Modelling*, 12(1):1–22, 2015.

[63] Otoniel Rodríguez-Jorge, Linda A Kempis-Calanis, Wassim Abou-Jaoudé, Darely Y Gutiérrez-Reyna, Céline Hernandez, Oscar Ramirez-Pliego, Morgane Thomas-Chollier, Salvatore Spicuglia, Maria A Santana, and Denis Thieffry. Cooperation between t cell receptor and toll-like receptor 5 signaling for cd4+ t cell activation. *Science signaling*, 12(577):eaar3641, 2019.

[64] Anke Ryll, Regina Samaga, Fred Schaper, Leonidas G Alexopoulos, and Steffen Klamt. Large-scale network models of IL-1 and IL-6 signalling and their hepatocellular specification. *Molecular Biosystems*, 7(12):3253–3270, 2011.

[65] Assieh Saadatpour, Rui-Sheng Wang, Aijun Liao, Xin Liu, Thomas P Loughran, István Albert, and Réka Albert. Dynamical and structural analysis of a t cell survival network identifies novel candidate therapeutic targets for large granular lymphocyte leukemia. *PLoS computational biology*, 7(11):e1002267, 2011.

[66] Julio Saez-Rodriguez, Luca Simeoni, Jonathan A Lindquist, Rebecca Hemenway, Ursula Bommhardt, Boerge Arndt, Utz-Uwe Haus, Robert Weismantel, Ernst D Gilles, Steffen Klamt, et al. A logical model provides insights into T cell receptor signaling. *PLoS computational biology*, 3(8):e163, 2007.

[67] Özgür Sahin, Holger Fröhlich, Christian Löbke, Ulrike Korf, Sara Burmester, Meher Majety, Jens Mattern, Ingo Schupp, Claudine Chaouiya, Denis Thieffry, et al. Modeling erbb receptor-regulated g1/s transition to find novel targets for de novo trastuzumab resistance. *BMC systems biology*, 3(1):1–20, 2009.

[68] Regina Samaga, Julio Saez-Rodriguez, Leonidas G Alexopoulos, Peter K Sorger, and Steffen Klamt. The logic of EGFR/ErbB signaling: theoretical properties and analysis of high-throughput data. *PLoS computational biology*, 5(8):e1000438, 2009.

[69] Ismael Sánchez-Osorio, Carlos A Hernández-Martínez, and Agustino Martínez-Antonio. Modeling asymmetric cell division in caulobacter crescentus using a boolean logic approach. In *Asymmetric Cell Division in Development, Differentiation and Cancer*, pages 1–21. Springer, 2017.

[70] Rafael Silva-Rocha and Víctor de Lorenzo. The tol network of p seudomonas putida mt-2 processes multiple environmental inputs into a narrow response space. *Environmental microbiology*, 15(1):271–286, 2013.

[71] Amit Singh, Juliana M Nascimento, Silke Kowar, Hauke Busch, and Melanie Boerries. Boolean approach to signalling pathway modelling in hgf-induced keratinocyte migration. *Bioinformatics*, 28(18):i495–i501, 2012.

[72] Sriram Sridharan, Ritwik Layek, Aniruddha Datta, and Jijayanagaram Venkatraj. Boolean modeling and fault diagnosis in oxidative stress response. *BMC genomics*, 13(6):1–16, 2012.

[73] Steven N Steinway, Matthew B Biggs, Thomas P Loughran Jr, Jason A Papin, and Reka Albert. Inference of network dynamics and metabolic interactions in the gut microbiome. *PLoS computational biology*, 11(6):e1004338, 2015.

[74] Juilee Thakar, Ashutosh K Pathak, Lisa Murphy, Réka Albert, and Isabella M Cattadori. Network model of immune responses reveals key effectors to single and co-infection dynamics by a respiratory bacterium and a gastrointestinal helminth. *PLoS computational biology*, 8(1):e1002345, 2012.

[75] Robert G Todd and Tomáš Helikar. Ergodic sets as cell phenotype of budding yeast cell cycle. 2012.

[76] Alan Veliz-Cuba and Brandilyn Stigler. Boolean models can explain bistability in the lac operon. *Journal of computational biology*, 18(6):783–794, 2011.

[77] Loic Verlingue, Aurélien Dugourd, Gautier Stoll, Emmanuel Barillot, Laurence Calzone, and Arturo Londoño-Vallejo. A comprehensive approach to the molecular determinants of lifespan using a boolean model of geroconversion. *Aging cell*, 15(6):1018–1026, 2016.

[78] Ranran Zhang, Mithun Vinod Shah, Jun Yang, Susan B Nyland, Xin Liu, Jong K Yun, Réka Albert, and Thomas P Loughran. Network model of survival signaling in large granular lymphocyte leukemia. *Proceedings of the National Academy of Sciences*, 105(42):16308–16313, 2008.