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 [31] or GINsim [59]. 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 [39], `aeon` format as used in AEON [5], and the universal SBML-qual [8] 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	[66, 31]
002	SIGNAL TRANSDUCTION IN FIBROBLASTS	130	9	557	[30, 31]
003	MAMMALIAN CELL CYCLE	19	1	51	[74, 31]
004	ERBB RECEPTOR SIGNALING	225	22	1100	[29, 31]
005	FA/BRCA PATHWAY	28	0	123	[68, 31]
006	HGF SIGNALING IN KERATINOCYTES	62	6	103	[78, 31]
007	CORTICAL AREA DEVELOPMENT	5	0	14	[23, 31]
008	DEATH RECEPTOR SIGNALING	25	3	45	[7, 31]
009	YEAST APOPTOSIS	60	13	114	[36, 31]
010	CARDIAC-DEVELOPMENT	13	2	37	[32, 31]
011	GUARD CELL ABSCISIC ACID SIGNALING	40	4	78	[42, 31]
012	T-CELL RECEPTOR SIGNALING	94	7	158	[73, 31]
013	CHOLESTEROL REGULATORY PATHWAY	32	2	41	[37, 31]
014	T-LGL SURVIVAL NETWORK 2008	54	7	193	[87, 31]
015	NEUROTRANSMITTER SIGNALING PATHWAY	14	2	20	[27, 31]
016	IL-1 SIGNALING	104	14	218	[71, 31]
017	DIFFERENTIATION OF T-LYMPHOCYTES	41	9	97	[50, 31]
018	EGFR-ERBB SIGNALING	76	28	226	[75, 31]
019	IL-6 SIGNALING	71	15	149	[71, 31]
020	APOPTOSIS NETWORK	39	2	73	[46, 31]
021	BODY SEGMENTATION IN DROSOPHILA 2013	14	3	29	[48, 31]
022	B-CELL DIFFERENTIATION	17	5	39	[53, 31]
023	MAMMALIAN CELL CYCLE 2006	9	1	34	[20, 31]
024	BUDDING YEAST CELL CYCLE	16	4	42	[83, 31]
025	T-LGL SURVIVAL NETWORK 2011	54	6	195	[72, 31]
026	BUDDING YEAST CELL CYCLE 2009	18	0	59	[33, 31]
027	WG PATHWAY OF DROSOPHILA	12	14	29	[52, 31]
028	VEGF PATHWAY OF DROSOPHILA	10	8	18	[52, 31]
029	TOLL PATHWAY OF DROSOPHILA	9	2	11	[52, 31]
030	SPZ NETWORK OF DROSOPHILA	18	6	28	[52, 31]

ID	Name	Vars.	Inps.	Regs.	Source
031	CELL CYCLE TRANSCRIPTION	9	0	19	[62, 31]
032	T-CELL SIGNALLING 2006	37	3	53	[38, 31]
033	BT474 BREAST CELL LINE LONG TERM	19	5	68	[18, 31]
034	HCC1954 BREAST CELL LINE LONG TERM	19	4	68	[18, 31]
035	BT474 BREAST CELL LINE SHORT TERM	11	5	46	[18, 31]
036	HCC1954 BREAST CELL LINE SHORT TERM	11	5	46	[18, 31]
037	SKBR3 BREAST CELL LINE SHORT TERM	11	5	41	[18, 31]
038	SKBR3 BREAST CELL LINE LONG TERM	21	4	81	[18, 31]
039	HIV-1 INTERACTIONS WITH T-CELL SIGNALING	124	14	368	[65, 31]
040	T-CELL DIFFERENTIATION	19	4	34	[55, 31]
041	INFLUENZA VIRUS REPLICATION CYCLE	120	11	302	[45, 31]
042	TOL REGULATORY NETWORK	14	10	48	[77, 31]
043	BORDETELLA BRONCHISEPTICA	33	0	79	[82, 31]
044	TRICHOSTRONGYLUS RETORTAEFORMIS	25	1	58	[82, 31]
045	HH PATHWAY OF DROSOPHILA	11	13	32	[52, 31]
046	B BRONCHISEPTICA AND T RETORTAEFORMIS	52	1	135	[82, 31]
047	FGF PATHWAY OF DROSOPHILA	14	9	24	[52, 31]
048	GLUCOSE REPRESSION SIGNALING 2009	55	18	97	[10, 31]
049	OXIDATIVE STRESS PATHWAY	18	1	32	[79, 31]
050	CD4 T-CELL SIGNALING	154	34	351	[14, 31]
051	COLITIS ASSOCIATED COLON CANCER	69	1	153	[43, 31]
052	SEPTATION INITIATION NETWORK	23	8	50	[9, 31]
053	PREDICTING VARIABILITIES IN CARDIAC GENE	13	2	37	[25, 31]
054	PC12 CELL DIFFERENTIATION	61	1	108	[60, 31]
055	HUMAN GONADAL SEX DETERMINATION	19	0	79	[67, 31]
056	IGVH MUTATIONS IN LYMPHOCYTIC LEUKEMIA	66	25	125	[1, 31]

ID	Name	Vars.	Inps.	Regs.	Source
057	FANCONI ANEMIA AND CHECKPOINT RECOVERY	15	0	66	[69, 31]
058	ARABIDOPSIS THALIANA CELL CYCLE	14	0	66	[63, 31]
059	BORTEZOMIB RESPONSES IN MYELOMA CELLS	62	5	131	[11, 31]
060	STOMATAL OPENING	44	5	167	[22, 31]
061	TUMOR MICROENVIRONMENT IN LYMPHOBLASTIC LEUKAEMIA	24	2	79	[19, 31]
062	CD4 T-CELL DIFFERENTIATION AND PLASTICITY	12	6	78	[49, 31]
063	LAC OPERON	10	3	22	[85, 31]
064	METABOLIC INTERACTIONS IN GUT MICROBIOME	8	4	27	[80, 31]
065	TUMOUR CELL INVASION AND MIGRATION	30	2	156	[12, 31]
066	CD4 T-CELL DIFFERENTIATION	29	9	96	[31]
067	REGULATION OF L-ARABINOSE OPERON	9	4	18	[35, 31]
068	AURORA KINASE-A IN NEUROBLASTOMA	19	4	43	[16, 31]
069	IRON ACQUISITION AND STRESS RESPONSE	20	2	38	[6, 31]
070	MAPK CANCER CELL FATE	49	4	104	[26, 31]
071	CASTRATION RESISTANT PROSTATE CANCER	28	14	51	[2, 31]
072	LYMPHOPOIESIS REGULATORY NETWORK	67	14	160	[54, 31]
073	LYMPHOID AND MYELOID CELL SPECIFICATION	31	2	94	[13, 31]
074	T-LGL SURVIVAL NETWORK 2011 REDUCED	18	0	43	[72, 31]
075	INFLAMMATORY BOWEL DISEASE	47	0	287	[4, 31]
076	SENESCENCE ASSOCIATED SECRETORY PHENOTYPE	49	2	96	[56, 31]
077	SIGNALLING PATHWAY FOR BUTANOL PRODUCTION	53	13	139	[58, 31]
078	IMMUNE SYSTEM	151	13	506	[31]
079	----	–	–	–	–
080	TCR SIGNALING 2018	95	15	212	[70, 59]
081	TLR5 SIGNALING 2018	40	2	68	[70, 59]
082	TCR-TLR5 SIGNALING 2018	112	16	257	[70, 59]
083	SIGNALING IN PROSTATE CANCER	122	11	420	[57, 59]
084	----	–	–	–	–
085	----	–	–	–	–

ID	Name	Vars.	Inps.	Regs.	Source
086	TUMOUR CELL INVASION AND MIGRATION REDUCED	18	2	88	[12, 59]
087	----	–	–	–	–
088	MIR-9 NEUROGENESIS	6	0	11	[15, 59]
089	MAPK REDUCED 1	13	4	78	[26, 59]
090	MAPK REDUCED 2	14	4	60	[26, 59]
091	MAPK REDUCED 3	12	4	58	[26, 59]
092	----	–	–	–	–
093	IMMUNE CHECKPOINT INHIBITORS	51	15	128	[40, 59]
094	----	–	–	–	–
095	FISSION YEAST 2008	9	1	27	[17, 59]
096	ERBB REGULATED G1-S TRANSITION	19	1	48	[34, 59]
097	DROSOPHILA WINGS AP	8	2	14	[24, 59]
098	----	–	–	–	–
099	----	–	–	–	–
100	----	–	–	–	–
101	----	–	–	–	–
102	----	–	–	–	–
103	----	–	–	–	–
104	DROSOPHILA CELL CYCLE	11	3	42	[21, 59]
105	----	–	–	–	–
106	----	–	–	–	–
107	----	–	–	–	–
108	GEROCONVERSION	23	2	67	[86, 59]
109	ASYMMETRIC CELL DIVISION A	5	0	15	[76, 59]
110	ASYMMETRIC CELL DIVISION B	9	0	12	[76, 59]
111	APOPTOSIS	18	15	40	[64]
112	COAGULATION PATHWAY	85	27	195	[64]
113	ER STRESS	107	75	266	[64]
114	ETC	46	38	154	[64]
115	E PROTEIN	17	18	40	[64]
116	HMOX1 PATHWAY	89	55	228	[64]
117	IFN LAMBDA	28	19	52	[64]
118	INTERFERON 1	66	55	190	[64]
119	JNK PATHWAY	13	6	21	[64]
120	KYNURENINE PATHWAY	78	72	304	[64]
121	NLRP3 ACTIVATION	39	18	91	[64]
122	NSP14	74	94	558	[64]
123	NSP4 NSP6	43	17	62	[64]
124	NSP9 PROTEIN	119	133	257	[64]
125	ORF10 CUL2 PATHWAY	34	17	92	[64]

ID	Name	Vars.	Inps.	Regs.	Source
126	ORF3A	24	18	56	[64]
127	PAMP SIGNALING	44	35	109	[64]
128	PYRIMIDINE DEPRIVATION	56	34	131	[64]
129	RTC AND TRANSCRIPTION	33	1	40	[64]
130	RENIN ANGIOTENSIN	43	34	130	[64]
131	TGFB PATHWAY	7	14	24	[64]
132	VIRUS REPLICATION CYCLE	129	19	268	[64]
133	ROOT STEM CELL 2010	8	2	16	[3, 47]
134	----	–	–	–	–
135	SIGNAL TRANSDUCTION	28	2	33	[44, 47]
136	EGF TNF ALPHA SIGNALLING PATHWAY	26	2	31	[8, 47]
137	SIGNALLING IN LIVER CANCER	71	11	118	[81, 47]
138	----	–	–	–	–
139	ACUTE RESPONSES DURING HYPERINSULINEMIA	10	9	64	[61, 47]
140	----	–	–	–	–
141	HIGH OSMOLARITY AND MATING PATHWAYS	43	2	94	[84, 47]
142	BLOOD STEM CELL	27	2	126	[28, 47]
143	----	–	–	–	–
144	----	–	–	–	–
145	MELANOGENESIS	61	1	113	[41]
167	MESODERM SPECIFICATION IN DROSOPHILA	41	16	130	[51, 47, 59]

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