Biodivne Boolean Models: A Comprehensive Logical Modelling Benchmark

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Abstract

The space of powerful tools for computational analysis of logical models (represented as Boolean networks) has been growing considerably in the recent years. However, comparing the validity, efficiency, and scalability of such tools necessitates a comprehensive benchmark set of realistic Boolean networks.

At the moment, this need is largely served by databases of biological models such as CellCollective, GINsim, or Biomodels. However, these databases are more focused on human curated, biologically relevant networks, and are therefore limited in scope. Furthermore, the models in such databases may not always be available as a single dataset or in the desired format. This requires additional time for preprocessing and data collection, which the tool authors are often unwilling or unable to spend.

In this technical report, we describe a comprehensive, open-source benchmark dataset that has been created by surveying the aforementioned databases, as well as a large body of other literature to obtain as many realistic 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 logically consistent using an automated static-analysis workflow. At the moment of writing, the dataset comprises more than 210 networks.

1 Introduction

Logical models provide a very useful and simple framework for describing complex biological phenomena. Likely the most common mechanism for formalising executable logical models are Boolean networks [130]. 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 [55], GINsim [97], or Biomodels [79]. However, these models are often hard to obtain in bulk or may require additional processing (e.g. to convert into an appropriate format). Additionally, publication authors often modify the models in

minor ways (e.g. by tweaking valuations of network inputs), which prevents meaningful comparisons between publications. 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. In this technical report, we describe a comprehensive, open-source benchmark dataset that can be used for this purpose instead.

Disclaimer: The model dataset as well as this report will be gradually updated as new models and data become available. If possible, please refer to the latest version of this report on arXiv and the latest revision of the dataset in the Github repository.

2 Goals and scope

Eligible models To cover the widest possible assortment of realistic models, we currently allow submission of any logical model which can be reliably retrieved from a known database, repository, or an associated publication. The only requirement is that the model must be based on a real biological system. That is, we do not accept randomly generated models. However, we do not require any specific level of curation either—the model can be hand made, automatically synthesised, or anything in between. Similarly, we accept many different model formats and we are willing to assist with translation if a machine-friendly format is not available. We also accept multi-valued models, however, for now the dataset only contains their Booleanized derivatives.

Editions The goal is to gradually evolve the dataset by adding new models (or by removing problematic/redundant models). Consequently, we plan to regularly release *editions* of the dataset, such that the users can refer to the whole history of editions as necessary. Preliminary plan is to release editions in roughly yearly intervals. Initially, editions will be available as Github releases, with a possible future addition of Zenodo artefacts. In each edition, the user can then pick models with specific properties (size, keywords, source, etc.).

Model metadata While we do not perform any biological curation of models, we collect basic meta-data about each model to make filtering and search easier. In particular, each model has:

- A numeric identifier that is unique within a specific dataset edition.
- A human-readable name. For simplicity, the name is limited to numbers, capital letters and the dash symbol (e.g. MODEL-NAME-5). To improve legibility, we may use spaces instead of dashes in text that is not meant to be machine readable (i.e. MODEL NAME 5).

- The DOI of the associated publication and its bibliographic entry (in Bibtex). Note that a single publication can contain multiple models—some DOIs thus appear in relation to multiple models.
- The URL where the model data was downloaded. This can be a list of URLs if the model is available from multiple sources. This can also be the publication DOI if the model is available directly through the published supplementary data.
- Basic structural metadata, such as the number of model *variables*, *inputs*, and *regulations*. The plan is to also incorporate additional structural measures of the regulatory graph later (e.g. feedback-vertex-set, SCC sizes, etc.), once additional static analysis steps are added.
- A set of curated *keywords*. Generally, these represent additional technical metadata, such as listing the databases where the model is available, or whether the model is based on multi-valued logic. At the moment, the dataset does not contain any biological keywords (e.g. cancer, differentiation, etc.). However, we are open to incorporating any community suggestions for additional keywords.
- A markdown document with any additional notes or relevant information about the model.

For each model, the metadata is summarised in a human-readable markdown README.md file, as well as a machine-readable .json document.

Contributions The dataset is managed using a versioned Github repository. Submitting a new model into the collection can be thus performed by anyone using the pull-request functionality (project readme has more detailed instructions about preparing such pull requests). Alternatively, we also accept submissions using issues: Simply create an issue with the bibliographic entry of the model you wish to include and we will try to incorporate it as soon as possible.

3 Technical information

The dataset is organized as follows:

- /models contains the whole dataset with all model and metadata files.
- /sources directory contains the original machine-readable source files that
 are used to generate the models directory.
- /report directory contains the LaTeX source files for this report.
- /sync.py is a Python script for model processing and static analysis (takes models from /sources and generates files in /models).

¹https://github.com/sybila/biodivine-boolean-models/

• /bundle.py is a Python script for creating model bundle archives. These can include model variants with different input representation, or a subset of the collection filtered according to some basic conditions.

For more information on how to use sync.py and bundle.py to work with the dataset, see the project readme file.

Keywords The metadata for each model can contain a set of keywords. In theory, any keyword can be added to identify specific classes of models. However, at the moment, we specifically recognise the following keywords:

- curated: A curated model is not only based on biological information, but is also (partially) validated by a human. That is, a model resulting from a purely automatic translation or inference can be included in the dataset, but is not automatically considered curated.
- repaired: A model where one or more logical inconsistencies have been resolved (a complete list of possible repairs is given later in this report). The rationale behind each modification should be listed in model notes.
- multi-valued: A model whose original version is multi-valued, but which is presented in a Booleanized form (the original multi-valued model should be included in the sources directory).
- cell-collective/ginsim/biomodels/covid-disease-map: Indicates that the model is available in the corresponding database (or multiple databases).
- casq: Indicates that the model has been translated from a CellDesigner pathway using the CaSQ tool [3].

Formats and representation At the moment, we support three major model formats for BN representation:

- .bnet; a simple plaintext file with the logical update functions [68].
- .aeon; also a plaintext format, but one that also incorporates the regulatory network of the model (with monotonicity and essentiality) [10].
- .sbml; XML-based format with support for additional meta-data (model layout, entity references and comments, etc.) [14].

Each model is available in all three formats. Any of the three formats can be also used as a model source (however, only limited static analysis is available for .bnet models due to the missing regulatory network). To ensure compatibility across all tools, we also perform model variable renaming when necessary. For example, .sbml supports (almost) arbitrary strings as variable names, while other formats follow a more typical C-like naming requirements. As such, regardless of the source format, variable names are normalized so that they are valid in any format.

Model inputs We also normalize the representation of model inputs and constants. Formally, an input or a constant is an entity with no incoming regulations, and either an identity (input) or true/false (constant) update function. The update function for inputs can be also missing entirely to indicate that the value is unknown/undetermined.

The specific representation of such variables is typically at the discretion of the model authors and differs from model to model. For example, some authors use constant update functions for inputs with a "typical" or "assumed" value, while other authors use the identity function, and other authors omit the functions entirely, only describing the expected values in text.

To make the resulting models as canonical as possible, we opted to *omit the update function* for every constant or input variable. If you wish to use the original setting as published by the authors, this information is still available in the /sources directory, or as part of the original publication. Furthermore, using the bundle.py script, you can generate variants of the dataset with a different input setting (constant true/constant false/identity function/free).

For benchmarking and tool comparison, we generally recommend sampling a non-trivial subspace of input valuations, as the behaviour of the model can often differ substantially based on the values of inputs. The model with all input values erased is therefore a good starting point for such sampling.

Multi-valued networks Some logical models are not Boolean, but multi-valued. Our dataset also includes models of this type. However, every such model is only given in the Booleanized format where the multi-valued entities are expanded into multiple Boolean variables. At the moment, the Booleanization is performed manually using the GINsim [97] software. In the future, we may include this as an automated step in the analysis workflow. Every Booleanized multi-valued model is marked with the multi-valued keyword. The original multi-valued model is also available in the corresponding sources sub-directory.

Duplicates Some models are available from multiple sources (typically multiple model databases). To eliminate duplicates, we typically only include a single version of the same model, but list multiple model URLs as possible sources (note that different databases can sometimes have slightly different versions of the same model). The information about duplicates and model-database mapping is also tracked in a shared spreadsheet.² Note that some publications can still contain multiple models, in which case we include all such models (each model is linked to the single shared publication). Similarly, multiple publications can describe variations or derivatives of a single model. We then typically include the variations as separate models, as long as there is a non-trivial difference from the original model (e.g. new/removed variables or regulations).

 $^{^2} https://docs.google.com/spreadsheets/d/1YFMaT3SKOwsReW3r6umv7Atqjoe1AZJmeMQ3HBPnIUI/edit?usp=sharing$

Model repair Many published models contain logical inconsistencies that we are able to detect as part of our static analysis workflow. Such issues have to be resolved before the model can be included in the dataset. For every model where such "repair" operation was performed, we use the repaired keyword and describe the repair process in the model notes. Furthermore, the original (unaltered) model file should be available in the sources directory. In general, we recognise the following types of problems:

- Monotonicity: When a model declares a regulation as (positively or negatively) monotonous, but the actual update function does not adhere to this assumption, we remove the monotonicity requirement from the regulation.
- Essentiality: When a model declares a regulation but the regulator has no impact on the output of the update function, we mark the regulation as non-essential. This problem has two variants: Either the regulator is completely unused (in which case this is likely the intention of the model author), or the regulator appears in the update function, but has no actual impact on its output (in which case it is likely that the model author was not aware of this problem).
- Redundant variables: We expect the dependency graph of each model to be weakly connected, or at least to not contain completely disconnected variables. If such variables are found, they are removed.
- Typos and other issues: Sometimes, the logical inconsistency is due to an obvious typo in the model specification (e.g. substitution of two similar variable names), in which case we fix the typo to the best of our ability.

The goal of each repair is to retain the original update functions of the model (as these are typically crucial for reproducibility). We thus typically adjust the regulatory network to match the actual update functions.

4 Models

In the rest of the report, we give a complete enumeration of all models included in the dataset with basic metadata and associated bibliographic entries. A machine readable (.csv) version of this summary is available as part of each dataset edition.

ID	Name	Vars.	Inps.	Regs.	Source
001	SIGNALING IN MACROPHAGE ACTIVATION	302	19	533	[111]
002	SIGNAL TRANSDUCTION IN FIBROBLASTS	130	9	557	[54]
003	MAMMALIAN CELL CYCLE	19	1	51	[121]
004	ERBB RECEPTOR SIGNALING	225	22	1100	[53]
005	FA/BRCA PATHWAY	28	0	123	[115]
006	HGF SIGNALING IN KERATINOCYTES	62	6	103	[135]
007	CORTICAL AREA DEVELOPMENT	5	0	14	[38]
008	DEATH RECEPTOR SIGNALING	25	3	45	[13]
009	YEAST APOPTOSIS	60	13	114	[64]
010	CARDIAC-DEVELOPMENT	13	2	37	[59]
011	GUARD CELL ABSCISIC ACID SIGNALING	40	4	78	[71]
012	T-CELL RECEPTOR SIGNALING	94	7	158	[120]
013	CHOLESTEROL REGULATORY PATHWAY	32	2	41	[65]
014	T-LGL SURVIVAL NETWORK 2008	54	7	193	[152]
015	NEUROTRANSMITTER SIGNALING PATHWAY	14	2	20	[50]
016	IL-1 SIGNALING	104	14	218	[118]
017	DIFFERENTIATION OF T-LYMPHOCYTES	41	9	97	[83]
018	EGFR-ERBB SIGNALING	76	28	226	[122]
019	IL-6 SIGNALING	71	15	149	[118]
020	APOPTOSIS NETWORK	39	2	73	[78]
021	BODY SEGMENTATION IN DROSOPHILA 2013	14	3	29	[81]
022	B-CELL DIFFERENTIATION	17	5	39	[86]
023	MAMMALIAN CELL CYCLE 2006	9	1	34	[30]
024	BUDDING YEAST CELL CYCLE	16	4	42	[143]
025	T-LGL SURVIVAL NETWORK 2011	54	6	195	[119]
026	BUDDING YEAST CELL CYCLE 2009	18	0	59	[60]
027	WG PATHWAY OF DROSOPHILA	12	14	29	[85]
028	VEGF PATHWAY OF DROSOPHILA	10	8	18	[85]
029	TOLL PATHWAY OF DROSOPHILA	9	2	11	[85]
030	SPZ NETWORK OF DROSOPHILA	18	6	28	[85]

ID	Name	Vars.	Inps.	Regs.	Source
031	CELL CYCLE TRANSCRIPTION	9	0	19	[103]
032	T-CELL SIGNALLING 2006	37	3	53	[67]
033	BT474 BREAST CELL LINE LONG TERM	19	5	68	[27]
034	HCC1954 BREAST CELL LINE LONG TERM	19	4	68	[27]
035	BT474 BREAST CELL LINE SHORT TERM	11	5	46	[27]
036	HCC1954 BREAST CELL LINE SHORT TERM	11	5	46	[27]
037	SKBR3 BREAST CELL LINE SHORT TERM	11	5	41	[27]
038	SKBR3 BREAST CELL LINE LONG TERM	21	4	81	[27]
039	HIV-1 INTERACTIONS WITH T-CELL SIGNALING	124	14	368	[106]
040	T-CELL DIFFERENTIATION	19	4	34	[90]
041	INFLUENZA VIRUS REPLICATION CYCLE	120	11	302	[75]
042	TOL REGULATORY NETWORK	14	10	48	[133]
043	BORDETELLA BRONCHISEPTICA	33	0	79	[141]
044	TRICHOSTRONGYLUS RETORTAEFORMIS	25	1	58	[141]
045	HH PATHWAY OF DROSOPHILA	11	13	32	[85]
046	B BRONCHISEPTICA AND T RETORTAEFORMIS	52	1	135	[141]
047	FGF PATHWAY OF DROSOPHILA	14	9	24	[85]
048	GLUCOSE REPRESSION SIGNALING 2009	55	18	97	[17]
049	OXIDATIVE STRESS PATHWAY	18	1	32	[137]
050	CD4 T-CELL SIGNALING	154	34	351	[21]
051	COLITIS ASSOCIATED COLON CANCER	69	1	153	[72]
052	SEPTATION INITIATION NETWORK	23	8	50	[15]
053	PREDICTING VARIABILITIES IN CARDIAC GENE	13	2	37	[43]
054	PC12 CELL DIFFERENTIATION	61	1	108	[101]
055	HUMAN GONADAL SEX DETERMINATION	19	0	79	[114]
056	IGVH MUTATIONS IN LYMPHOCYTIC LEUKEMIA	66	25	125	[5]

ID	Name	Vars.	Inps.	Regs.	Source
057	FANCONI ANEMIA AND CHECKPOINT RECOVERY	15	0	66	[116]
058	ARABIDOPSIS THALIANA CELL CYCLE	14	0	66	[104]
059	BORTEZOMIB RESPONSES IN MYELOMA CELLS	62	5	131	[18]
060	STOMATAL OPENING	44	5	167	[36]
061	TUMOR MICROENVIRONMENT IN LYMPHOBLASTIC LEUKAEMIA	24	2	79	[29]
062	CD4 T-CELL DIFFERENTIATION AND PLASTICITY	12	6	78	[82]
063	LAC OPERON	10	3	22	[147]
064	METABOLIC INTERACTIONS IN GUT MICROBIOME	8	4	27	[138]
065	TUMOUR CELL INVASION AND MIGRATION	30	2	156	[19]
066	CD4 T-CELL DIFFERENTIATION	29	9	96	[55]
067	REGULATION OF L-ARABINOSE OPERON	9	4	18	[62]
068	AURORA KINASE-A IN NEUROBLASTOMA	19	4	43	[24]
069	IRON ACQUISITION AND STRESS RESPONSE	20	2	38	[11]
070	MAPK CANCER CELL FATE	49	4	104	[44]
071	CASTRATION RESISTANT PROSTATE CANCER	28	14	51	[6]
072	LYMPHOPOIESIS REGULATORY NETWORK	67	14	160	[89]
073	LYMPHOID AND MYELOID CELL SPECIFICATION	31	2	94	[20]
074	T-LGL SURVIVAL NETWORK 2011 REDUCED	18	0	43	[119]
075	INFLAMMATORY BOWEL DISEASE	47	0	287	[8]
076	SENESCENCE ASSOCIATED SECRETORY PHENOTYPE	49	2	96	[91]
077	SIGNALLING PATHWAY FOR BUTANOL PRODUCTION	53	13	139	[95]
078	IMMUNE SYSTEM	151	13	506	[55]
079	COLORECTAL TUMORIGENESIS	184	13	747	[16]
080	TCR SIGNALING 2018	95	15	212	[117]
081	TLR5 SIGNALING 2018	40	2	68	[117]
082	TCR-TLR5 SIGNALING 2018	112	16	257	[117]
083	SIGNALING IN PROSTATE CANCER	122	11	420	[94]

ID	Name	Vars.	Inps.	Regs.	Source
084	ABA INDUCED STOMATAL CLOSURE	58	23	155	[4]
085	REPROGRAMMING TESTES DERIVED STEM CELLS	23	4	49	[51]
086	TUMOUR CELL INVASION AND MIGRATION REDUCED	18	2	88	[19]
087	INFLAMMATORY GENE EXPRESSION IN MACROPHAGES	99	34	190	[113]
088	MIR-9 NEUROGENESIS	6	0	11	[22]
089	MAPK REDUCED 1	13	4	78	[44]
090	MAPK REDUCED 2	14	4	60	[44]
091	MAPK REDUCED 3	12	4	58	[44]
092	HEPATOCELLULAR CARCINOMA	61	8	139	[139]
093	IMMUNE CHECKPOINT INHIBITORS	51	15	128	[69]
094	MACROPHAGE POLARIZATION STATES	23	8	52	[108]
095	FISSION YEAST 2008	9	1	27	[25]
096	ERBB REGULATED G1-S TRANSITION	19	1	48	[61]
097	DROSOPHILA WINGS AP	8	2	14	[41]
098	MACROPHAGE POLARIZATION EXTENDED	30	12	72	[80]
099	YEAST HYPHAL TRANSITION	16	3	36	[150]
100	ACUTE MYELOID LEUKEMIA	18	3	30	[107]
101	GUARD CELL CO2 SIGNALLING	61	24	155	[63]
102	PANCREATIC CANCER MICROENVIRONMENT REDUCED	17	5	52	[110]
103	PANCREATIC CANCER MICROENVIRONMENT	65	4	110	[110]
104	DROSOPHILA CELL CYCLE	11	3	42	[32]
105	PLANT GUARD CELL SIGNALLING	46	3	113	[77]
106	STOMATAL RESTING STATE	58	22	151	[76]
107	DNA DAMAGE INDUCED AUTOPHAGY	32	1	99	[49]
108	GEROCONVERSION	23	2	67	[148]
109	ASYMMETRIC CELL DIVISION A	5	0	15	[128]
110	ASYMMETRIC CELL DIVISION B	9	0	12	[128]
111	APOPTOSIS	18	15	40	[105]
112	COAGULATION PATHWAY	85	27	195	[105]
113	ER STRESS	107	75	266	[105]
114	ETC	46	38	154	[105]
115	E PROTEIN	17	18	40	[105]
116	HMOX1 PATHWAY	89	55	228	[105]
117	IFN LAMBDA	28	19	52	[105]
118	INTERFERON 1	66	55	190	[105]

ID	Name	Vars.	Inps.	Regs.	Source
119	JNK PATHWAY	13	6	21	[105]
120	KYNURENINE PATHWAY	78	72	304	[105]
121	NLRP3 ACTIVATION	39	18	91	[105]
122	NSP14	74	94	558	[105]
123	NSP4 NSP6	43	17	62	[105]
124	NSP9 PROTEIN	119	133	257	[105]
125	ORF10 CUL2 PATHWAY	34	17	92	[105]
126	ORF3A	24	18	56	[105]
127	PAMP SIGNALING	44	35	109	[105]
128	PYRIMIDINE DEPRIVATION	56	34	131	[105]
129	RTC AND TRANSCRIPTION	33	1	40	[105]
130	RENIN ANGIOTENSIN	43	34	130	[105]
131	TGFB PATHWAY	7	14	24	[105]
132	VIRUS REPLICATION CYCLE	129	19	268	[105]
133	ROOT STEM CELL 2010	8	2	16	[7]
134	RHEUMATOID ARTHRITIS	35	3	59	[92]
135	SIGNAL TRANSDUCTION	28	2	33	[74]
136	EGF TNF ALPHA SIGNALLING PATHWAY	26	2	31	[14]
137	SIGNALLING IN LIVER CANCER	71	11	118	[140]
138	APOPTOSIS-UPDATED	17	14	37	[37]
139	ACUTE RESPONSES DURING HYPERINSULINEMIA	10	9	64	[102]
140	BREAST CANCER DRUG RESISTANCE	62	18	211	[40]
141	HIGH OSMOLARITY AND MATING PATHWAYS	43	2	94	[146]
142	BLOOD STEM CELL	27	2	126	[52]
143	BREAST CANCER INHIBITORS	71	26	223	[39]
144	SNF1-AMPK-PATHWAY	146	56	482	[73]
145	MELANOGENESIS	61	1	113	[70]
146	BUDDING YEAST FAURE 2009	40	10	271	[31]
147	BUDDING YEAST EXIT MODULE	11	5	44	[31]
148	AGS CELL FATE DECISION	83	0	185	[34]
149	AGS CELL FATE DECISION REDUCED	12	2	62	[34]
150	CELL FATE DECISION MULTISCALE	31	2	52	[13]
151	TCR REDOX METABOLISM	130	3	417	[129]
152	TCR REDOX METABOLISM REDUCED	50	3	288	[129]
153	CONTROL OF PROLIFERATION	17	1	34	[151]
154	CONTROL OF TH1 TH2 DIFFERENTIATION	18	3	50	[88]

ID	Name	Vars.	Inps.	Regs.	Source
155	CONTROL OF TH1 TH2 TH17 TREG DIFFERENTATION	45	26	164	[96]
156	CONTROL OF TH1 TH2 TH17 TREG DIFFERENTATION REDUCED	23	13	108	[96]
157	CONTROL OF TH DIFFERENTATION	62	41	234	[1]
158	LAMBDA PHAGE LYSOGENY	7	0	30	[142]
159	BUDDING YEAST CORE	31	8	158	[31]
160	IL17 DIFFERENTIAL EXPRESSION	76	16	246	[23]
161	DIFFERENTIATION OF MONOCYTES	94	2	244	[100]
162	DROSOPHILA DPP PATHWAY	10	8	40	[85]
163	DROSOPHILA EGF PATHWAY	24	10	84	[85]
164	EGGSHELL PATTERNING MECHANISTIC	17	7	62	[33]
165	EGGSHELL PATTERNING PHENOMOENOLOGICAL	4	4	16	[33]
166	DROSOPHILA JAK STAT PATHWAY	7	12	36	[85]
167	MESODERM SPECIFICATION IN DROSOPHILA	41	16	130	[84]
168	DROSOPHILA NOTCH PATHWAY	7	6	26	[85]
169	DROSOPHILA GAP A	5	2	17	[126]
170	DROSOPHILA GAP B	4	3	15	[126]
171	DROSOPHILA GAP C	5	2	20	[126]
172	DROSOPHILA GAP D	5	2	12	[126]
173	GLUCOSE REPRESSION SIGNALLING	62	14	116	[17]
174	HEPATOCELLULAR CARCINOMA REDUCED	19	0	71	[139]
175	SEA URCHIN	32	9	95	[35]
176	MYELOFIBROTIC MICROENVIRONMENT	47	2	148	[28]
177	LYMPHOID CELL SPECIFICATION	31	3	96	[20]
178	MAST CELL ACTIVATION	45	3	72	[98]
179	MICROENVIRONMENT CONTROL	46	10	149	[131]
180	MORPHOGENETIC CHECKPOINT	11	1	36	[31]
181	MULTILEVEL CELL CYCLE	12	1	59	[144]
182	BOOLEAN CELL CYCLE	12	2	59	[144]
183	ALTERATIONS IN BLADDER	31	4	111	[112]
184	P53 MDM2 NETWORK	5	1	15	[2]
185	CHICKEN SEX DETERMINATION	12	3	34	[124]

ID	Name	Vars.	Inps.	Regs.	Source
186	CHICKEN SEX DETERMINATION REDUCED	7	3	25	[124]
187	MAMMAL SEX DETERMINATION 1 CELL	13	6	55	[123]
188	MAMMAL SEX DETERMINATION 2 CELL	30	7	132	[123]
189	TRP BIOSYNTHESIS	5	1	13	[134]
190	BRAF TREATMENT RESPONSE	32	5	74	[9]
191	SEGMENT POLARITY 1 CELL	17	2	55	[125]
192	SEGMENT POLARITY 6 CELL	102	0	352	[125]
193	SENESCENCE G1S CHECKPOINT	28	2	100	[93]
194	VULVAR PRECURSOR CELLS	78	28	236	[149]
195	CTLA4 PD1 CHECKPOINT INHIBITORS	161	55	439	[58]
196	T-LYMPHOCYTE SPECIFICATION	58	3	237	[12]
197	ANTERIOR POSTERIOR BOUNDARY	48	8	253	[42]
198	PAIR RULE MODULE	11	0	48	[127]
199	HEPATOCELLULAR CARCINOMA COMPARTMENTALIZED	30	0	97	[87]
200	LUNG-CANCER-CELL-CYCLE	25	1	71	[48]
201	ONKOGENE ROLE OF INCRNA ANRIL	31	2	94	[45]
202	ONKOGENE ROLE OF INCRNA XIST	30	1	107	[47]
203	DDR SIGNALLING PATHWAYS	39	1	143	[46]
204	HUMAN BRAIN ORGANOIDS	76	1	205	[109]
205	EPITHELIAL-MESENCHYMAL TRANSITION IN BLADDER	41	4	118	[66]
206	EPITHELIAL-MESENCHYMAL TRANSITION IN BREAST	36	5	97	[66]
207	BREAST CANCER TUMOUR	85	18	441	[132]
208	HEMATOPOIESIS AGING	15	0	36	[57]
209	ABERRANT CELL CYCLE PROGRESSION	85	2	372	[136]
210	DRUG SYNERGY PREDICTION	144	0	367	[99]
211	EPITHELIAL-DERIVED CANCER CELLS	183	0	602	[145]
212	ESCHERICHIA COLI TRYPTOPHAN	13	3	27	[26]
213	DOPAMINE TRANSCRIPTION	54	11	94	[56]
214	FOXO3 PATHWAY	52	18	89	[56]
215	MTOR PATHWAY	41	26	83	[56]
216	PPARGC1A PATHWAY	52	17	109	[56]
217	PRKN PATHWAY	21	35	72	[56]
218	TCA CYCLE	34	34	197	[56]

ID	Name	Vars.	Inps.	Regs.	Source
219	WNT-PI3K-AKT PATHWAY	45	39	106	[56]

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