

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 [45] or GINsim [77]. 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 [54], **aeon** format as used in AEON [9], and the universal SBML-qual [13] 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 | [86, 45] |
| 002 | SIGNAL TRANSDUCTION IN FIBROBLASTS | 130 | 9 | 557 | [44, 45] |
| 003 | MAMMALIAN CELL CYCLE | 19 | 1 | 51 | [96, 45] |
| 004 | ERBB RECEPTOR SIGNALING | 225 | 22 | 1100 | [43, 45] |
| 005 | FA/BRCA PATHWAY | 28 | 0 | 123 | [90, 45] |
| 006 | HGF SIGNALING IN KERATINOCYTES | 62 | 6 | 103 | [108, 45] |
| 007 | CORTICAL AREA DEVELOPMENT | 5 | 0 | 14 | [35, 45] |
| 008 | DEATH RECEPTOR SIGNALING | 25 | 3 | 45 | [12, 45] |
| 009 | YEAST APOPTOSIS | 60 | 13 | 114 | [51, 45] |
| 010 | CARDIAC-DEVELOPMENT | 13 | 2 | 37 | [47, 45] |
| 011 | GUARD CELL ABSCISIC ACID SIGNALING | 40 | 4 | 78 | [57, 45] |
| 012 | T-CELL RECEPTOR SIGNALING | 94 | 7 | 158 | [95, 45] |
| 013 | CHOLESTEROL REGULATORY PATHWAY | 32 | 2 | 41 | [52, 45] |
| 014 | T-LGL SURVIVAL NETWORK 2008 | 54 | 7 | 193 | [121, 45] |
| 015 | NEUROTRANSMITTER SIGNALING PATHWAY | 14 | 2 | 20 | [40, 45] |
| 016 | IL-1 SIGNALING | 104 | 14 | 218 | [93, 45] |
| 017 | DIFFERENTIATION OF T-LYMPHOCYTES | 41 | 9 | 97 | [65, 45] |
| 018 | EGFR-ERBB SIGNALING | 76 | 28 | 226 | [97, 45] |
| 019 | IL-6 SIGNALING | 71 | 15 | 149 | [93, 45] |
| 020 | APOPTOSIS NETWORK | 39 | 2 | 73 | [61, 45] |
| 021 | BODY SEGMENTATION IN DROSOPHILA 2013 | 14 | 3 | 29 | [63, 45] |
| 022 | B-CELL DIFFERENTIATION | 17 | 5 | 39 | [68, 45] |
| 023 | MAMMALIAN CELL CYCLE 2006 | 9 | 1 | 34 | [28, 45] |
| 024 | BUDDING YEAST CELL CYCLE | 16 | 4 | 42 | [114, 45] |
| 025 | T-LGL SURVIVAL NETWORK 2011 | 54 | 6 | 195 | [94, 45] |
| 026 | BUDDING YEAST CELL CYCLE 2009 | 18 | 0 | 59 | [48, 45] |
| 027 | WG PATHWAY OF DROSOPHILA | 12 | 14 | 29 | [67, 45] |
| 028 | VEGF PATHWAY OF DROSOPHILA | 10 | 8 | 18 | [67, 45] |
| 029 | TOLL PATHWAY OF DROSOPHILA | 9 | 2 | 11 | [67, 45] |
| 030 | SPZ NETWORK OF DROSOPHILA | 18 | 6 | 28 | [67, 45] |

| ID | Name | Vars. | Inps. | Regs. | Source |
|-----|---|-------|-------|-------|--------------|
| 031 | CELL CYCLE TRANSCRIPTION | 9 | 0 | 19 | [82, 45] |
| 032 | T-CELL SIGNALLING 2006 | 37 | 3 | 53 | [53, 45] |
| 033 | BT474 BREAST CELL LINE LONG TERM | 19 | 5 | 68 | [25, 45] |
| 034 | HCC1954 BREAST CELL LINE LONG TERM | 19 | 4 | 68 | [25, 45] |
| 035 | BT474 BREAST CELL LINE SHORT TERM | 11 | 5 | 46 | [25, 45] |
| 036 | HCC1954 BREAST CELL LINE SHORT TERM | 11 | 5 | 46 | [25, 45] |
| 037 | SKBR3 BREAST CELL LINE SHORT TERM | 11 | 5 | 41 | [25, 45] |
| 038 | SKBR3 BREAST CELL LINE LONG TERM | 21 | 4 | 81 | [25, 45] |
| 039 | HIV-1 INTERACTIONS WITH T-CELL SIGNALING | 124 | 14 | 368 | [85, 45] |
| 040 | T-CELL DIFFERENTIATION | 19 | 4 | 34 | [71, 45] |
| 041 | INFLUENZA VIRUS REPLICATION CYCLE | 120 | 11 | 302 | [60, 45] |
| 042 | TOL REGULATORY NETWORK | 14 | 10 | 48 | [106, 45] |
| 043 | BORDETELLA BRONCHISEPTICA | 33 | 0 | 79 | [112, 45] |
| 044 | TRICHOSTRONGYLUS RETORTAEFORMIS | 25 | 1 | 58 | [112, 45] |
| 045 | HH PATHWAY OF DROSOPHILA | 11 | 13 | 32 | [67, 45] |
| 046 | B BRONCHISEPTICA AND T RETORTAEFORMIS | 52 | 1 | 135 | [112, 45] |
| 047 | FGF PATHWAY OF DROSOPHILA | 14 | 9 | 24 | [67, 45] |
| 048 | GLUCOSE REPRESSION SIGNALING 2009 | 55 | 18 | 97 | [16, 45] |
| 049 | OXIDATIVE STRESS PATHWAY | 18 | 1 | 32 | [109, 45] |
| 050 | CD4 T-CELL SIGNALING | 154 | 34 | 351 | [20, 45] |
| 051 | COLITIS ASSOCIATED COLON CANCER | 69 | 1 | 153 | [58, 45] |
| 052 | SEPTATION INITIATION NETWORK | 23 | 8 | 50 | [14, 45] |
| 053 | PREDICTING VARIABILITIES IN CARDIAC GENE | 13 | 2 | 37 | [38, 45] |
| 054 | PC12 CELL DIFFERENTIATION | 61 | 1 | 108 | [80, 45] |
| 055 | HUMAN GONADAL SEX DETERMINATION | 19 | 0 | 79 | [89, 45] |
| 056 | IGVH MUTATIONS IN LYMPHOCYTIC LEUKEMIA | 66 | 25 | 125 | [4, 45] |

| ID | Name | Vars. | Inps. | Regs. | Source |
|-----|---|-------|-------|-------|-----------|
| 057 | FANCONI ANEMIA AND CHECKPOINT RECOVERY | 15 | 0 | 66 | [91, 45] |
| 058 | ARABIDOPSIS THALIANA CELL CYCLE | 14 | 0 | 66 | [83, 45] |
| 059 | BORTEZOMIB RESPONSES IN MYELOMA CELLS | 62 | 5 | 131 | [17, 45] |
| 060 | STOMATAL OPENING | 44 | 5 | 167 | [34, 45] |
| 061 | TUMOR MICROENVIRONMENT IN LYMPHOBLASTIC LEUKAEMIA | 24 | 2 | 79 | [27, 45] |
| 062 | CD4 T-CELL DIFFERENTIATION AND PLASTICITY | 12 | 6 | 78 | [64, 45] |
| 063 | LAC OPERON | 10 | 3 | 22 | [117, 45] |
| 064 | METABOLIC INTERACTIONS IN GUT MICROBIOME | 8 | 4 | 27 | [110, 45] |
| 065 | TUMOUR CELL INVASION AND MIGRATION | 30 | 2 | 156 | [18, 45] |
| 066 | CD4 T-CELL DIFFERENTIATION | 29 | 9 | 96 | [45] |
| 067 | REGULATION OF L-ARABINOSE OPERON | 9 | 4 | 18 | [50, 45] |
| 068 | AURORA KINASE-A IN NEUROBLASTOMA | 19 | 4 | 43 | [23, 45] |
| 069 | IRON ACQUISITION AND STRESS RESPONSE | 20 | 2 | 38 | [10, 45] |
| 070 | MAPK CANCER CELL FATE | 49 | 4 | 104 | [39, 45] |
| 071 | CASTRATION RESISTANT PROSTATE CANCER | 28 | 14 | 51 | [5, 45] |
| 072 | LYMPHOPOIESIS REGULATORY NETWORK | 67 | 14 | 160 | [70, 45] |
| 073 | LYMPHOID AND MYELOID CELL SPECIFICATION | 31 | 2 | 94 | [19, 45] |
| 074 | T-LGL SURVIVAL NETWORK 2011 REDUCED | 18 | 0 | 43 | [94, 45] |
| 075 | INFLAMMATORY BOWEL DISEASE | 47 | 0 | 287 | [7, 45] |
| 076 | SENESCENCE ASSOCIATED SECRETORY PHENOTYPE | 49 | 2 | 96 | [72, 45] |
| 077 | SIGNALLING PATHWAY FOR BUTANOL PRODUCTION | 53 | 13 | 139 | [75, 45] |
| 078 | IMMUNE SYSTEM | 151 | 13 | 506 | [45] |
| 079 | COLORECTAL TUMORIGENESIS | 184 | 13 | 747 | [15] |
| 080 | TCR SIGNALING 2018 | 95 | 15 | 212 | [92, 77] |
| 081 | TLR5 SIGNALING 2018 | 40 | 2 | 68 | [92, 77] |
| 082 | TCR-TLR5 SIGNALING 2018 | 112 | 16 | 257 | [92, 77] |
| 083 | SIGNALING IN PROSTATE CANCER | 122 | 11 | 420 | [74, 77] |

| ID | Name | Vars. | Inps. | Regs. | Source |
|-----|--|-------|-------|-------|--------------|
| 084 | ABA INDUCED STOMATAL CLOSURE | 58 | 23 | 155 | [3] |
| 085 | REPROGRAMMING TESTES DERIVED STEM CELLS | 23 | 4 | 49 | [41] |
| 086 | TUMOUR CELL INVASION AND MIGRATION REDUCED | 18 | 2 | 88 | [18, 77] |
| 087 | INFLAMMATORY GENE EXPRESSION IN MACROPHAGES | 99 | 34 | 190 | [88] |
| 088 | MIR-9 NEUROGENESIS | 6 | 0 | 11 | [21, 77] |
| 089 | MAPK REDUCED 1 | 13 | 4 | 78 | [39, 77] |
| 090 | MAPK REDUCED 2 | 14 | 4 | 60 | [39, 77] |
| 091 | MAPK REDUCED 3 | 12 | 4 | 58 | [39, 77] |
| 092 | ---- | — | — | — | — |
| 093 | IMMUNE CHECKPOINT INHIBITORS | 51 | 15 | 128 | [55, 77] |
| 094 | ---- | — | — | — | — |
| 095 | FISSION YEAST 2008 | 9 | 1 | 27 | [24, 77] |
| 096 | ERBB REGULATED G1-S TRANSITION | 19 | 1 | 48 | [49, 77] |
| 097 | DROSOPHILA WINGS AP | 8 | 2 | 14 | [36, 77] |
| 098 | ---- | — | — | — | — |
| 099 | ---- | — | — | — | — |
| 100 | ---- | — | — | — | — |
| 101 | ---- | — | — | — | — |
| 102 | ---- | — | — | — | — |
| 103 | ---- | — | — | — | — |
| 104 | DROSOPHILA CELL CYCLE | 11 | 3 | 42 | [30, 77] |
| 105 | ---- | — | — | — | — |
| 106 | ---- | — | — | — | — |
| 107 | ---- | — | — | — | — |
| 108 | GEROCONVERSION | 23 | 2 | 67 | [118, 77] |
| 109 | ASYMMETRIC CELL DIVISION A | 5 | 0 | 15 | [103, 77] |
| 110 | ASYMMETRIC CELL DIVISION B | 9 | 0 | 12 | [103, 77] |
| 111 | APOPTOSIS | 18 | 15 | 40 | [84] |
| 112 | COAGULATION PATHWAY | 85 | 27 | 195 | [84] |
| 113 | ER STRESS | 107 | 75 | 266 | [84] |
| 114 | ETC | 46 | 38 | 154 | [84] |
| 115 | E PROTEIN | 17 | 18 | 40 | [84] |
| 116 | HMOX1 PATHWAY | 89 | 55 | 228 | [84] |
| 117 | IFN LAMBDA | 28 | 19 | 52 | [84] |
| 118 | INTERFERON 1 | 66 | 55 | 190 | [84] |
| 119 | JNK PATHWAY | 13 | 6 | 21 | [84] |
| 120 | KYNURENINE PATHWAY | 78 | 72 | 304 | [84] |
| 121 | NLRP3 ACTIVATION | 39 | 18 | 91 | [84] |

| ID | Name | Vars. | Inps. | Regs. | Source |
|-----|--|-------|-------|-------|--------------|
| 122 | NSP14 | 74 | 94 | 558 | [84] |
| 123 | NSP4 NSP6 | 43 | 17 | 62 | [84] |
| 124 | NSP9 PROTEIN | 119 | 133 | 257 | [84] |
| 125 | ORF10 CUL2 PATHWAY | 34 | 17 | 92 | [84] |
| 126 | ORF3A | 24 | 18 | 56 | [84] |
| 127 | PAMP SIGNALING | 44 | 35 | 109 | [84] |
| 128 | PYRIMIDINE DEPRIVATION | 56 | 34 | 131 | [84] |
| 129 | RTC AND TRANSCRIPTION | 33 | 1 | 40 | [84] |
| 130 | RENIN ANGIOTENSIN | 43 | 34 | 130 | [84] |
| 131 | TGFB PATHWAY | 7 | 14 | 24 | [84] |
| 132 | VIRUS REPLICATION CYCLE | 129 | 19 | 268 | [84] |
| 133 | ROOT STEM CELL 2010 | 8 | 2 | 16 | [6, 62] |
| 134 | ---- | — | — | — | — |
| 135 | SIGNAL TRANSDUCTION | 28 | 2 | 33 | [59, 62] |
| 136 | EGF TNF ALPHA SIGNALLING PATHWAY | 26 | 2 | 31 | [13, 62] |
| 137 | SIGNALLING IN LIVER CANCER | 71 | 11 | 118 | [111, 62] |
| 138 | ---- | — | — | — | — |
| 139 | ACUTE RESPONSES DURING HYPERINSULINEMIA | 10 | 9 | 64 | [81, 62] |
| 140 | ---- | — | — | — | — |
| 141 | HIGH OSMOLARITY AND MATING PATHWAYS | 43 | 2 | 94 | [116, 62] |
| 142 | BLOOD STEM CELL | 27 | 2 | 126 | [42, 62] |
| 143 | ---- | — | — | — | — |
| 144 | ---- | — | — | — | — |
| 145 | MELANOGENESIS | 61 | 1 | 113 | [56] |
| 146 | BUDDING YEAST FAURE 2009 | 40 | 10 | 271 | [29, 77] |
| 147 | BUDDING YEAST EXIT MODULE | 11 | 5 | 44 | [29, 77] |
| 148 | AGS CELL FATE DECISION | 83 | 0 | 185 | [32, 77] |
| 149 | AGS CELL FATE DECISION REDUCED | 12 | 2 | 62 | [32, 77] |
| 150 | CELL FATE DECISION MULTISCALE | 31 | 2 | 52 | [12, 77] |
| 151 | TCR REDOX METABOLISM | 130 | 3 | 417 | [104, 77] |
| 152 | TCR REDOX METABOLISM REDUCED | 50 | 3 | 288 | [104, 77] |
| 153 | CONTROL OF PROLIFERATION | 17 | 1 | 34 | [120, 77] |
| 154 | CONTROL OF TH1 TH2 DIFFERENTIATION | 18 | 3 | 50 | [69, 77] |

| ID | Name | Vars. | Inps. | Regs. | Source |
|-----|--|-------|-------|-------|--------------|
| 155 | CONTROL OF TH1 TH2 TH17 TREG DIFFERENTIATION | 45 | 26 | 164 | [76, 77] |
| 156 | CONTROL OF TH1 TH2 TH17 TREG DIFFERENTIATION REDUCED | 23 | 13 | 108 | [76, 77] |
| 157 | CONTROL OF TH DIFFERENTIATION | 62 | 41 | 234 | [1, 77] |
| 158 | LAMBDA PHAGE LYSOGENY | 7 | 0 | 30 | [113, 77] |
| 159 | BUDDING YEAST CORE | 31 | 8 | 158 | [29, 77] |
| 160 | IL17 DIFFERENTIAL EXPRESSION | 76 | 16 | 246 | [22, 77, 62] |
| 161 | DIFFERENTIATION OF MONOCYTES | 94 | 2 | 244 | [79, 77] |
| 162 | DROSOPHILA DPP PATHWAY | 10 | 8 | 40 | [67, 77] |
| 163 | DROSOPHILA EGF PATHWAY | 24 | 10 | 84 | [67, 77] |
| 164 | EGGSHELL PATTERNING MECHANISTIC | 17 | 7 | 62 | [31, 77] |
| 165 | EGGSHELL PATTERNING PHENOMENOLOGICAL | 4 | 4 | 16 | [31, 77] |
| 166 | DROSOPHILA JAK STAT PATHWAY | 7 | 12 | 36 | [67, 77] |
| 167 | MESODERM SPECIFICATION IN DROSOPHILA | 41 | 16 | 130 | [66, 62, 77] |
| 168 | DROSOPHILA NOTCH PATHWAY | 7 | 6 | 26 | [67, 77] |
| 169 | DROSOPHILA GAP A | 5 | 2 | 17 | [101, 77] |
| 170 | DROSOPHILA GAP B | 4 | 3 | 15 | [101, 77] |
| 171 | DROSOPHILA GAP C | 5 | 2 | 20 | [101, 77] |
| 172 | DROSOPHILA GAP D | 5 | 2 | 12 | [101, 77] |
| 173 | ---- | | | | |
| 174 | ---- | | | | |
| 175 | SEA URCHIN | 32 | 9 | 95 | [33, 77, 62] |
| 176 | MYELOFIBROTIC MICROENVIRONMENT | 47 | 2 | 148 | [26, 77] |
| 177 | LYMPHOID CELL SPECIFICATION | 31 | 3 | 96 | [19, 77] |
| 178 | MAST CELL ACTIVATION | 45 | 3 | 72 | [78, 77] |
| 179 | MICROENVIRONMENT CONTROL | 46 | 10 | 149 | [105, 77] |
| 180 | MORPHOGENETIC CHECKPOINT | 11 | 1 | 36 | [29, 77] |
| 181 | MULTILEVEL CELL CYCLE | 12 | 1 | 59 | [115, 77] |
| 182 | BOOLEAN CELL CYCLE | 12 | 2 | 59 | [115, 77] |
| 183 | ALTERATIONS IN BLADDER | 31 | 4 | 111 | [87, 77] |
| 184 | P53 MDM2 NETWORK | 5 | 1 | 15 | [2, 77] |
| 185 | CHICKEN SEX DETERMINATION ⁸ | 12 | 3 | 34 | [99, 77] |

| ID | Name | Vars. | Inps. | Regs. | Source |
|-----|-----------------------------------|-------|-------|-------|--------------|
| 186 | CHICKEN SEX DETERMINATION REDUCED | 7 | 3 | 25 | [99, 77] |
| 187 | MAMMAL SEX DETERMINATION 1 CELL | 13 | 6 | 55 | [98, 77] |
| 188 | MAMMAL SEX DETERMINATION 2 CELL | 30 | 7 | 132 | [98, 77] |
| 189 | TRP BIOSYNTHESIS | 5 | 1 | 13 | [107, 77] |
| 190 | BRAF TREATMENT RESPONSE | 32 | 5 | 74 | [8, 77] |
| 191 | SEGMENT POLARITY 1 CELL | 17 | 2 | 55 | [100, 77] |
| 192 | SEGMENT POLARITY 6 CELL | 102 | 0 | 352 | [100, 77] |
| 193 | SENESCENCE G1S CHECKPOINT | 28 | 2 | 100 | [73, 77] |
| 194 | VULVAR PRECURSOR CELLS | 78 | 28 | 236 | [119, 77] |
| 195 | CTLA4 PD1 CHECKPOINT INHIBITORS | 161 | 55 | 439 | [46, 77] |
| 196 | T-LYMPHOCYTE SPECIFICATION | 58 | 3 | 237 | [11, 77, 62] |
| 197 | ANTERIOR POSTERIOR BOUNDARY | 48 | 8 | 253 | [37, 77] |
| 198 | PAIR RULE MODULE | 11 | 0 | 48 | [102, 77] |
| 199 | ---- | – | – | – | – |
| 200 | ---- | – | – | – | – |
| ID | Name | Vars. | Inps. | Regs. | Source |

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