atlas Documentation

Rodrigo Santibáñez

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CONTENTS

Atlas is a small software developed to use simple text files that encode biological networks and write Rule-Based Models (RBMs). Atlas writes rules and others model components for the PySB python package PySB, PMID 23423320. The RBMs could be simulated within PySB with NFsim, PMID 26556387 (within the BioNetGen2 software, PMID 27402907), KaSim (KaSim, PMID 29950016). Models could be exported to text files in *BioNetGen* (BioNetGenLanguage) or *kappa* language (Kappa) for further calibration (BioNetFit, PMID 26556387 or pleione, PMID 31641245) and analysis (sterope for parameter sensibility and alcyone for parameter uncertainty).

CHAPTER

ONE

INSTALLATION

There are two different ways to install Atlas:

1. **Install Atlas natively (Recommended).**

   OR

2. **Clone the Github repository.** If you are familiar with git, Atlas can be cloned and the respective folder added to the python path. Further details are below.

Note: Need Help? If you run into any problems with installation, please visit our chat room: https://gitter.im/glucksfall/pleiades

1.1 Option 1: Install Atlas natively on your computer

The recommended approach is to use system tools, or install them if necessary. To install python packages, you could use pip, or download the package from the python package index.

1. **Install with system tools**

   With pip, you need to execute and Atlas will be installed on `$HOME/.local/lib/python3.6/site-packages` folder or similar.

   ```
   pip3 install atlas_rbm --user
   ```

   If you have system rights, you could install Atlas for all users with

   ```
   sudo -H pip3 install atlas_rbm
   ```

2. **Download from the python package index**

   Alternatively, you could download the package (useful when pip fails to download the package because of lack of SSL libraries) and then install with pip. For instance:

   ```
   wget https://files.pythonhosted.org/packages/ec/ed/
   ↪8b94e0a29f69a24ddb18ba4a4e6463d3ecede308576774e86baf6a84b998/atlas_rbm-1.0.2-
   ↪py3-none-any.whl
   pip3 install atlas_rbm-1.0.2-py3-none-any.whl --user
   ```

   Note: Why Python3?: Atlas is intended to be used with >=python3.4 because python2.7 won't receive further development past 2020, including security updates.

Note: pip, Python, and Anaconda: Be aware which pip you invoque. You could install pip3 with `sudo apt-get install python3-pip` if you have system rights, or install python3 from source, and adding `<python3 path>/bin/pip3` to the path, or linking it in a directory like `$HOME/bin` which is commonly added to the path at login. Also be aware that, if you installed Anaconda, pip could be linked to the Anaconda specific version of pip, which will install Atlas into Anaconda's installation folder. Type `which pip` or `which pip3` to find out the source of pip, and type `python -m site` or `python3 -m site` to find out where is more likely Atlas will be installed.

1.2 Option 2: Clone the Github repository

1. **Clone with git**

   The source code is uploaded and maintained through Github at https://github.com/networkbiolab/atlas. Therefore, you could clone the repository locally, and then add the folder to the `PYTHONPATH`. Beware that you should install the *pysb* package (pysb) and others packages by any means, specially the Jupyter Notebook project (https://jupyter.org).

```
path=/opt/atlas
git clone https://github.com/networkbiolab/atlas $path
echo export PYTHONPATH="\$PYTHONPATH:\$path" >> $HOME/.profile
```

Note: Adding the path to `$HOME/.profile` allows python to find the package installation folder after each user login. Similarly, adding the path to `$HOME/.bashrc` allows python to find the package after each terminal invocation. Other options include setting the `PYTHONPATH` environmental variable in a sh file (see the example folder) or invoke `python3 setup.py clean build install` to install Atlas as it was downloaded from the PyPI server.

CHAPTER

TWO

MODELING

Atlas is a modular software with each script centered in a specific biological network

1. *Metabolic Networks*
2. **Interaction Networks**
    1. *Protein-Protein Interaction Networks*
    2. *Protein-Small compounds Interaction Networks*
    3. **Protein-RNA Interaction Networks**
    4. **RNA-RNA Interaction Networks**
    5. *Transcription Factor-DNA Binding Site Interaction Networks*
    6. *Sigma Factor-Promoter Interaction Networks*
3. *Genome Graphs*

2.1 Metabolic Networks

Metabolic networks have four columns. The first declares a unique name for the enzyme or enzymatic complex; the second declares a unique name for the reaction; the third column lists using comma unique names for substrates; and the last row list using comma unique names for products. To declare metabolites located at the periplasm or extracellular compartments, the user should employ the prefix "PER-" and "EX-", respectively. Use *spontaneous* for non-enzymatic reactions.

Examples:

```
GENE        REACTION        SUBSTRATES        PRODUCTS
spontaneous        LACTOSE-MUTAROTATION        alpha-lactose        beta-lactose
spontaneous        GALACTOSE-MUTAROTATION        alpha-GALACTOSE        beta-GALACTOSE
spontaneous        GLUCOSE-MUTAROTATION        alpha-glucose        beta-glucose
LACY-MONOMER        TRANS-RXN-24        PER-PROTON, PER-alpha-lactose        PROTON, alpha-lactose
LACY-MONOMER        TRANS-RXN-24-beta        PER-PROTON, PER-beta-lactose        PROTON, beta-lactose
LACY-MONOMER        TRANS-RXN-94        PER-PROTON, PER-MELIBIOSE        PROTON, MELIBIOSE
LACY-MONOMER        RXN0-7215        PER-PROTON, PER-CPD-3561        PROTON, CPD-3561
LACY-MONOMER        RXN0-7217        PER-PROTON, PER-CPD-3785        PROTON, CPD-3785
LACY-MONOMER        RXN-17755        PER-PROTON, PER-CPD-3801        PROTON, CPD-3801
BETAGALACTOSID-CPLX        BETAGALACTOSID-RXN        beta-lactose, WATER        beta-GALACTOSE, beta-glucose
```

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```
BETAGALACTOSID-CPLX        BETAGALACTOSID-RXN-alpha        alpha-lactose, WATER        alpha-GALACTOSE, alpha-glucose
BETAGALACTOSID-CPLX        RXN0-5363        alpha-lactose        alpha-ALLOLACTOSE
BETAGALACTOSID-CPLX        RXN0-5363-beta        beta-lactose        beta-ALLOLACTOSE
BETAGALACTOSID-CPLX        ALLOLACTOSE-DEG-alpha        alpha-ALLOLACTOSE        alpha-GALACTOSE, alpha-glucose
BETAGALACTOSID-CPLX        ALLOLACTOSE-DEG-beta        beta-ALLOLACTOSE        beta-GALACTOSE, beta-glucose
BETAGALACTOSID-CPLX        RXN-17726        CPD-3561, WATER        beta-GALACTOSE, Fructofuranose
BETAGALACTOSID-CPLX        RXN0-7219        CPD-3785, WATER        beta-GALACTOSE, D-ARABINOSE
GALACTOACETYLTRAN-CPLX        GALACTOACETYLTRAN-RXN-galactose        beta-GALACTOSE, ACETYL-COA        6-Acetyl-beta-D-Galactose, CO-A
```

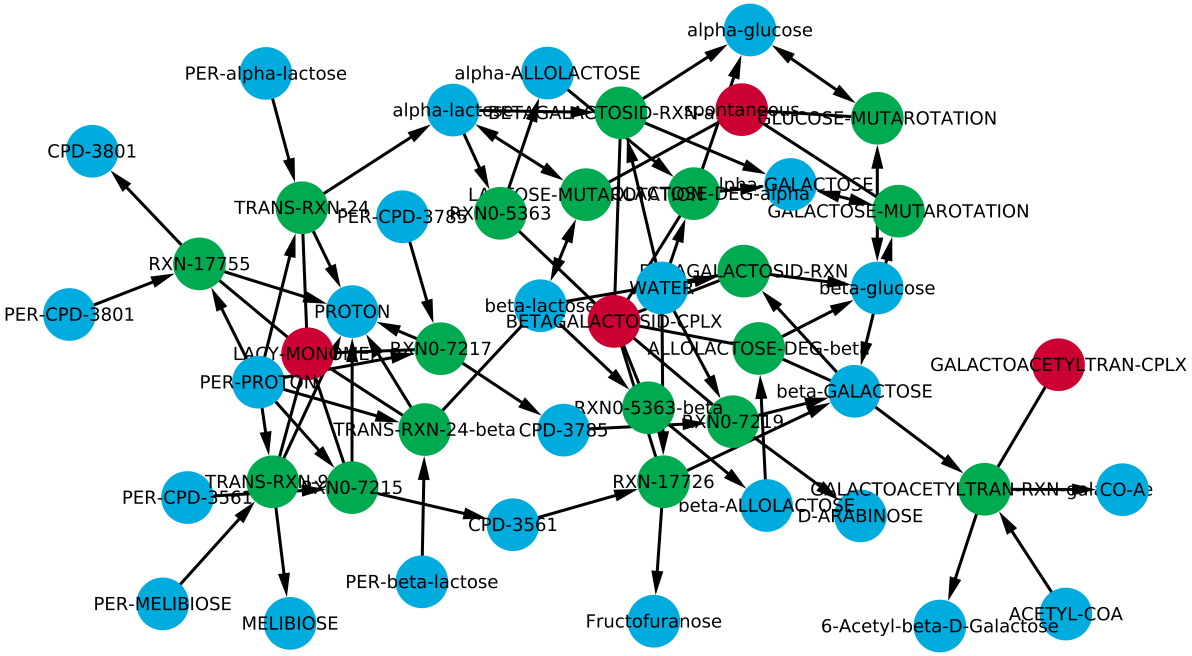
OR

```
GENE        REACTION        SUBSTRATES        PRODUCTS        FWD_RATE        RVS_RATE
spontaneous        LACTOSE-MUTAROTATION        alpha-lactose        beta-lactose        1.0        1.0
spontaneous        GALACTOSE-MUTAROTATION        alpha-GALACTOSE        beta-GALACTOSE        1.0        1.0
spontaneous        GLUCOSE-MUTAROTATION        alpha-glucose        beta-glucose        1.0        1.0
MEM-lacY        TRANS-RXN-24        PER-PROTON, PER-alpha-lactose        PROTON, alpha-lactose        1.0        0.0
MEM-lacY        TRANS-RXN-24-beta        PER-PROTON, PER-beta-lactose        PROTON, beta-lactose        1.0        0.0
MEM-lacY        TRANS-RXN-94        PER-PROTON, PER-MELIBIOSE        PROTON, MELIBIOSE        1.0        1.0
MEM-lacY        RXN0-7215        PER-PROTON, PER-CPD-3561        PROTON, CPD-3561        1.0        1.0
MEM-lacY        RXN0-7217        PER-PROTON, PER-CPD-3785        PROTON, CPD-3785        1.0        1.0
MEM-lacY        RXN-17755        PER-PROTON, PER-CPD-3801        PROTON, CPD-3801        1.0        1.0
lacZ        BETAGALACTOSID-RXN        beta-lactose, WATER        beta-GALACTOSE, beta-glucose        1.0        0.0
lacZ        BETAGALACTOSID-RXN-alpha        alpha-lactose, WATER        alpha-GALACTOSE, alpha-glucose        1.0        0.0
lacZ        RXN0-5363        alpha-lactose        alpha-ALLOLACTOSE        1.0        1.0
lacZ        RXN0-5363-beta        beta-lactose        beta-ALLOLACTOSE        1.0        1.0
lacZ        ALLOLACTOSE-DEG-alpha        alpha-ALLOLACTOSE, WATER        alpha-GALACTOSE, alpha-glucose        1.0        0.0
lacZ        ALLOLACTOSE-DEG-beta        beta-ALLOLACTOSE, WATER        beta-GALACTOSE, beta-glucose        1.0        0.0
lacZ        RXN-17726        CPD-3561, WATER        beta-GALACTOSE, Fructofuranose        1.0        1.0
lacZ        RXN0-7219        CPD-3785, WATER        beta-GALACTOSE, D-ARABINOSE        1.0        1.0
lacA        GALACTOACETYLTRAN-RXN-galactose        beta-GALACTOSE, ACETYL-COA        6-Acetyl-beta-D-Galactose, CO-A        1.0        1.0
```

OR

```
GENE        REACTION        SUBSTRATES        PRODUCTS        FWD_RATE        RVS_RATE
spontaneous        LACTOSE-MUTAROTATION        alpha-lactose        beta-
↪lactose        1.0        1.0
spontaneous        GALACTOSE-MUTAROTATION        alpha-GALACTOSE        beta-
↪GALACTOSE        1.0        1.0
spontaneous        GLUCOSE-MUTAROTATION        alpha-glucose        beta-
↪glucose        1.0        1.0
MEM-lacY        TRANS-RXN-24        PER-PROTON, PER-alpha-lactose        PROTON,␣
↪alpha-lactose        1.0        0.0
MEM-lacY        TRANS-RXN-24-beta        PER-PROTON, PER-beta-lactose        PROTON,␣
↪beta-lactose        1.0        0.0
MEM-lacY        TRANS-RXN-94        PER-PROTON, PER-MELIBIOSE        PROTON,␣
↪MELIBIOSE        1.0        1.0
MEM-lacY        RXN0-7215        PER-PROTON, PER-CPD-3561        PROTON, CPD-
↪3561        1.0        1.0
MEM-lacY        RXN0-7217        PER-PROTON, PER-CPD-3785        PROTON, CPD-
↪3785        1.0        1.0
MEM-lacY        RXN-17755        PER-PROTON, PER-CPD-3801        PROTON, CPD-
↪3801        1.0        1.0
[lacZ,lacZ,lacZ,lacZ]        BETAGALACTOSID-RXN        beta-lactose,␣
↪WATER        beta-GALACTOSE, beta-glucose        1.0        0.0
[lacZ,lacZ,lacZ,lacZ]        BETAGALACTOSID-RXN-alpha        alpha-lactose,␣
↪WATER        alpha-GALACTOSE, alpha-glucose        1.0        0.0
[lacZ,lacZ,lacZ,lacZ]        RXN0-5363        alpha-lactose        alpha-
↪ALLOLACTOSE        1.0        1.0
[lacZ,lacZ,lacZ,lacZ]        RXN0-5363-beta        beta-lactose        beta-
↪ALLOLACTOSE        1.0        1.0
[lacZ,lacZ,lacZ,lacZ]        ALLOLACTOSE-DEG-alpha        alpha-ALLOLACTOSE,␣
↪WATER        alpha-GALACTOSE, alpha-glucose        1.0        0.0
[lacZ,lacZ,lacZ,lacZ]        ALLOLACTOSE-DEG-beta        beta-ALLOLACTOSE,␣
↪WATER        beta-GALACTOSE, beta-glucose        1.0        0.0
[lacZ,lacZ,lacZ,lacZ]        RXN-17726        CPD-3561, WATER        beta-GALACTOSE,␣
↪Fructofuranose        1.0        1.0
[lacZ,lacZ,lacZ,lacZ]        RXN0-7219        CPD-3785, WATER        beta-GALACTOSE,␣
↪D-ARABINOSE        1.0        1.0
[lacA,lacA,lacA]        GALACTOACETYLTRAN-RXN-galactose        beta-GALACTOSE, ACETYL-
↪COA        6-Acetyl-beta-D-Galactose, CO-A        1.0        1.0
```

Note: Visualization in Cytoscape. Transform the four-columns file into a two-columns file with the helper script "*Expand metabolic network.ipynb*", paste the results in a new file, and import the network into Cytoscape. Colors and arrows remains to the user for customization.



Finally, execute the "*Rules from metabolic network.ipynb*" to obtain the *Rules* to model the defined metabolic network. The complete rule-based model can be found in the lactose folder from the Network Biology Lab GitHub repository here.

```
Rule('LACTOSE_MUTAROTATION',
        met(name = 'alpha_lactose', loc = 'cyt') |
        met(name = 'beta_lactose', loc = 'cyt'),
        Parameter('fwd_LACTOSE_MUTAROTATION', 1),
        Parameter('rvs_LACTOSE_MUTAROTATION', 1))

Rule('GALACTOSE_MUTAROTATION',
        met(name = 'alpha_GALACTOSE', loc = 'cyt') |
        met(name = 'beta_GALACTOSE', loc = 'cyt'),
        Parameter('fwd_GALACTOSE_MUTAROTATION', 1),
        Parameter('rvs_GALACTOSE_MUTAROTATION', 1))

Rule('GLUCOSE_MUTAROTATION',
        met(name = 'alpha_glucose', loc = 'cyt') |
        met(name = 'beta_glucose', loc = 'cyt'),
        Parameter('fwd_GLUCOSE_MUTAROTATION', 1),
        Parameter('rvs_GLUCOSE_MUTAROTATION', 1))

Rule('TRANS_RXN_24',
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'per') +
        met(name = 'alpha_lactose', loc = 'per') |
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'cyt') +
        met(name = 'alpha_lactose', loc = 'cyt'),
        Parameter('fwd_TRANS_RXN_24', 1),
        Parameter('rvs_TRANS_RXN_24', 1))

Rule('TRANS_RXN_24_beta',
```

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```
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'per') +
        met(name = 'beta_lactose', loc = 'per') |
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'cyt') +
        met(name = 'beta_lactose', loc = 'cyt'),
        Parameter('fwd_TRANS_RXN_24_beta', 1),
        Parameter('rvs_TRANS_RXN_24_beta', 1))

Rule('TRANS_RXN_94',
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'per') +
        met(name = 'MELIBIOSE', loc = 'per') |
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'cyt') +
        met(name = 'MELIBIOSE', loc = 'cyt'),
        Parameter('fwd_TRANS_RXN_94', 1),
        Parameter('rvs_TRANS_RXN_94', 1))

Rule('RXN0_7215', prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'per') +
        met(name = 'CPD_3561', loc = 'per') |
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'cyt') +
        met(name = 'CPD_3561', loc = 'cyt'),
        Parameter('fwd_RXN0_7215', 1),
        Parameter('rvs_RXN0_7215', 1))

Rule('RXN0_7217', prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'per') +
        met(name = 'CPD_3785', loc = 'per') |
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'cyt') +
        met(name = 'CPD_3785', loc = 'cyt'),
        Parameter('fwd_RXN0_7217', 1),
        Parameter('rvs_RXN0_7217', 1))

Rule('RXN_17755', prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'per') +
        met(name = 'CPD_3801', loc = 'per') |
        prot(name = 'LACY_MONOMER') +
        met(name = 'PROTON', loc = 'cyt') +
        met(name = 'CPD_3801', loc = 'cyt'),
        Parameter('fwd_RXN_17755', 1),
        Parameter('rvs_RXN_17755', 1))

Rule('BETAGALACTOSID_RXN',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_lactose', loc = 'cyt') +
        met(name = 'WATER', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_GALACTOSE', loc = 'cyt') +
        met(name = 'beta_glucose', loc = 'cyt'),
        Parameter('fwd_BETAGALACTOSID_RXN', 1),
        Parameter('rvs_BETAGALACTOSID_RXN', 1))

Rule('BETAGALACTOSID_RXN_alpha',
```

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```
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'alpha_lactose', loc = 'cyt') +
        met(name = 'WATER', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'alpha_GALACTOSE', loc = 'cyt') +
        met(name = 'alpha_glucose', loc = 'cyt'),
        Parameter('fwd_BETAGALACTOSID_RXN_alpha', 1),
        Parameter('rvs_BETAGALACTOSID_RXN_alpha', 1))

Rule('RXN0_5363',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'alpha_lactose', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'alpha_ALLOLACTOSE', loc = 'cyt'),
        Parameter('fwd_RXN0_5363', 1),
        Parameter('rvs_RXN0_5363', 1))

Rule('RXN0_5363_beta',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_lactose', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_ALLOLACTOSE', loc = 'cyt'),
        Parameter('fwd_RXN0_5363_beta', 1),
        Parameter('rvs_RXN0_5363_beta', 1))

Rule('ALLOLACTOSE_DEG_alpha',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'alpha_ALLOLACTOSE', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'alpha_GALACTOSE', loc = 'cyt'),
        Parameter('fwd_ALLOLACTOSE_DEG_alpha', 1),
        Parameter('rvs_ALLOLACTOSE_DEG_alpha', 1))

Rule('ALLOLACTOSE_DEG_beta',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_ALLOLACTOSE', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_GALACTOSE', loc = 'cyt'),
        Parameter('fwd_ALLOLACTOSE_DEG_beta', 1),
        Parameter('rvs_ALLOLACTOSE_DEG_beta', 1))

Rule('RXN_17726',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'CPD_3561', loc = 'cyt') +
        met(name = 'WATER', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_GALACTOSE', loc = 'cyt') +
        met(name = 'Fructofuranose', loc = 'cyt'),
        Parameter('fwd_RXN_17726', 1),
        Parameter('rvs_RXN_17726', 1))

Rule('RXN0_7219',
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'CPD_3785', loc = 'cyt') +
        met(name = 'WATER', loc = 'cyt') |
        cplx(name = 'BETAGALACTOSID_CPLX') +
        met(name = 'beta_GALACTOSE', loc = 'cyt') +
```

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```
        met(name = 'D_ARABINOSE', loc = 'cyt'),
        Parameter('fwd_RXN0_7219', 1),
        Parameter('rvs_RXN0_7219', 1))

Rule('GALACTOACETYLTRAN_RXN_galactose',
        cplx(name = 'GALACTOACETYLTRAN_CPLX') +
        met(name = 'beta_GALACTOSE', loc = 'cyt') +
        met(name = 'ACETYL_COA', loc = 'cyt') |
        cplx(name = 'GALACTOACETYLTRAN_CPLX') +
        met(name = '_6_Acetyl_beta_D_Galactose', loc = 'cyt') +
        met(name = 'CO_A', loc = 'cyt'),
        Parameter('fwd_GALACTOACETYLTRAN_RXN_galactose', 1),
        Parameter('rvs_GALACTOACETYLTRAN_RXN_galactose', 1))
```

Note: Reversibility of Rules. Atlas writes reversible *Rules* for each reaction declared in the network file. The `Parameter('rvs_RuleName', 1))` must be set to zero to define an irreversible reaction.

Note: Uniqueness of Rule names. Atlas will write *Rules* for unique metabolic reactions. Identical names will be reported for further curation.

Note: Simulation. The model can be simulated only with the instantiation of `Monomers` and `Initials` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the necessary `Monomers` and `Initials` (including proteins and enzymatic complexes).

Plotting. The model can be observed only with the instantation of `Observables` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the all possible `Observables` for metabolites.

2.2 Protein-Protein Interaction Networks

Protein-protein interaction (PPI) interaction networks have two columns. In any order and for any number of components, each column lists using comma the interacting proteins or protein complexes. The user should employ brackets to enclose a list of proteins that are part of a complex.

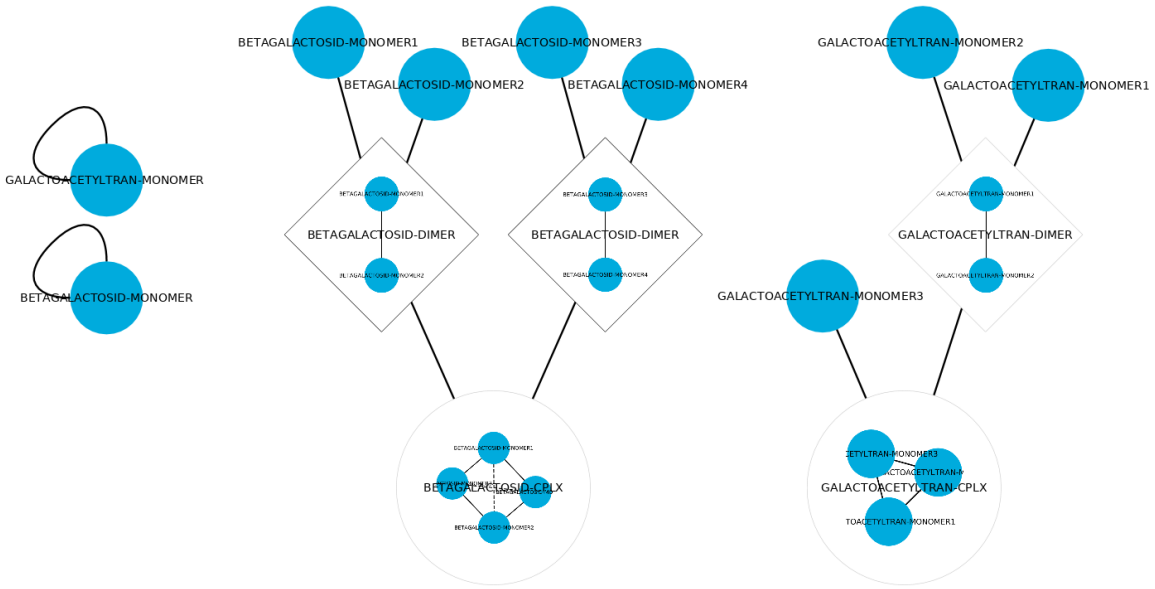
Examples:

```
SOURCE        TARGET
BETAGALACTOSID-MONOMER        BETAGALACTOSID-MONOMER
GALACTOACETYLTRAN-MONOMER        GALACTOACETYLTRAN-MONOMER
```

OR

```
SOURCE        TARGET
BETAGALACTOSID-MONOMER        BETAGALACTOSID-MONOMER
[BETAGALACTOSID-MONOMER, BETAGALACTOSID-MONOMER]        [BETAGALACTOSID-MONOMER,␣
↪BETAGALACTOSID-MONOMER]
GALACTOACETYLTRAN-MONOMER        GALACTOACETYLTRAN-MONOMER
GALACTOACETYLTRAN-MONOMER        [GALACTOACETYLTRAN-MONOMER, GALACTOACETYLTRAN-
↪MONOMER]
```

Note: Visualization in Cytoscape. Cytoscape cannot import hyper-graphs. To do so, Create simple network and right-click to embed a subnetwork in the corresponding node.



Finally, execute the "*Rules from protein-protein.ipynb*" to obtain the *Rules* to model the defined interaction network. The complete rule-based model can be found in the lactose folder from the Network Biology Lab GitHub repository here.

```
Rule('complex_assembly_rule_0',
        prot(name = 'BETAGALACTOSID_MONOMER', up = None, dw = None) +
        prot(name = 'BETAGALACTOSID_MONOMER', up = None, dw = None) |
        prot(name = 'BETAGALACTOSID_MONOMER', up = 1, dw = None) %
        prot(name = 'BETAGALACTOSID_MONOMER', up = None, dw = 1),
        Parameter('fwd_complex_assembly_rule_0', 1),
        Parameter('rvs_complex_assembly_rule_0', 0))

Rule('complex_assembly_rule_1',
        prot(name = 'BETAGALACTOSID_MONOMER', up = 1, dw = None) %
        prot(name = 'BETAGALACTOSID_MONOMER', up = None, dw = 1) +
        prot(name = 'BETAGALACTOSID_MONOMER', up = 1, dw = None) %
        prot(name = 'BETAGALACTOSID_MONOMER', up = None, dw = 1) |
        prot(name = 'BETAGALACTOSID_MONOMER', up = 1, dw = None) %
        prot(name = 'BETAGALACTOSID_MONOMER', up = 2, dw = 1) %
        prot(name = 'BETAGALACTOSID_MONOMER', up = 3, dw = 2) %
        prot(name = 'BETAGALACTOSID_MONOMER', up = None, dw = 3),
        Parameter('fwd_complex_assembly_rule_1', 1),
        Parameter('rvs_complex_assembly_rule_1', 0))

Rule('complex_assembly_rule_2',
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = None, dw = None) +
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = None, dw = None) |
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = 1, dw = None) %
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = None, dw = 1),
        Parameter('fwd_complex_assembly_rule_2', 1),
        Parameter('rvs_complex_assembly_rule_2', 0))

```

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```
Rule('complex_assembly_rule_3',
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = None, dw = None) +
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = 1, dw = None) %
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = None, dw = 1) |
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = 1, dw = None) %
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = 2, dw = 1) %
        prot(name = 'GALACTOACETYLTRAN_MONOMER', up = None, dw = 2),
        Parameter('fwd_complex_assembly_rule_3', 1),
        Parameter('rvs_complex_assembly_rule_3', 0))
```

Note: Reversibility of Rules. Atlas writes irreversible *Rules* for each reaction declared in the network file. The `Parameter('rvs_RuleName', 0))` must be set to non-zero to define an reversible reaction.

Note: Uniqueness of Rule names. Atlas will write *Rules* with numbered names. Use only one file to model the many interactions the system has.

Note: Simulation. The model can be simulated only with the instantiation of `Monomers` and `Initials` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the necessary `Monomers` and `Initials` (including proteins and enzymatic complexes). Manually add the necessary `Monomers` and `Initials` for non-enzymatic proteins.

Plotting. The model can be observed only with the instantation of `Observables` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the all possible `Observables` for enzymatic proteins. Other observables for proteins should be added manually.

2.3 Protein-Small compounds Interaction Networks

Protein-small compound interaction networks have two columns. Similar to a PPI network, but the user should add the prefix "SMALL-" to encode a small compound that interacts with the protein or protein complex.

Examples:

```
SOURCE        TARGET
PER-araF        SMALL-PER-alpha-L-arabinofuranose
PER-araF        SMALL-PER-beta-L-arabinofuranose
PER-araF        SMALL-PER-alpha-L-arabinopyranose
PER-araF        SMALL-PER-beta-L-arabinopyranose
[crp, crp]        SMALL-CAMP
[crp, SMALL-CAMP, crp]        SMALL-CAMP
[lacI, lacI]        SMALL-ALLOLACTOSE
[lacI, SMALL-ALLOLACTOSE, lacI]        SMALL-ALLOLACTOSE
[araG, araG]        SMALL-ATP
araC        SMALL-alpha-L-arabinopyranose
[araC, araC]        SMALL-alpha-L-arabinopyranose
[araC, SMALL-alpha-L-arabinopyranose, araC]        SMALL-alpha-L-arabinopyranose
```

Finally, execute the "*Rules from protein-small compounds.ipynb*" to obtain the *Rules* to model the defined interaction network. The complete rule-based model can be found in the arabinose folder from the Network Biology Lab GitHub repository here.

```
Rule('ProtMet_RuleAssembly_1',
        prot(name = 'araF', loc = 'per', met = None, up = None, dw = None) +
        met(name = 'alpha_L_arabinofuranose', loc = 'per', prot = None) |
        prot(name = 'araF', loc = 'per', met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinofuranose', loc = 'per', prot = 1),
        Parameter('fwd_ProtMet_RuleAssembly_1', 1),
        Parameter('rvs_ProtMet_RuleAssembly_1', 1))

Rule('ProtMet_RuleAssembly_2',
        prot(name = 'araF', loc = 'per', met = None, up = None, dw = None) +
        met(name = 'beta_L_arabinofuranose', loc = 'per', prot = None) |
        prot(name = 'araF', loc = 'per', met = 1, up = None, dw = None) %
        met(name = 'beta_L_arabinofuranose', loc = 'per', prot = 1),
        Parameter('fwd_ProtMet_RuleAssembly_2', 1),
        Parameter('rvs_ProtMet_RuleAssembly_2', 1))

Rule('ProtMet_RuleAssembly_3',
        prot(name = 'araF', loc = 'per', met = None, up = None, dw = None) +
        met(name = 'alpha_L_arabinopyranose', loc = 'per', prot = None) |
        prot(name = 'araF', loc = 'per', met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', loc = 'per', prot = 1),
        Parameter('fwd_ProtMet_RuleAssembly_3', 1),
        Parameter('rvs_ProtMet_RuleAssembly_3', 1))

Rule('ProtMet_RuleAssembly_4',
        prot(name = 'araF', loc = 'per', met = None, up = None, dw = None) +
        met(name = 'beta_L_arabinopyranose', loc = 'per', prot = None) |
        prot(name = 'araF', loc = 'per', met = 1, up = None, dw = None) %
        met(name = 'beta_L_arabinopyranose', loc = 'per', prot = 1),
        Parameter('fwd_ProtMet_RuleAssembly_4', 1),
        Parameter('rvs_ProtMet_RuleAssembly_4', 1))

Rule('ProtMet_RuleAssembly_5',
        prot(name = 'crp', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'crp', loc = 'cyt', met = None, up = 1, dw = None) +
        met(name = 'CAMP', loc = 'cyt', prot = None) |
        prot(name = 'crp', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'crp', loc = 'cyt', met = 2, up = 1, dw = None) %
        met(name = 'CAMP', loc = 'cyt', prot = 2),
        Parameter('fwd_ProtMet_RuleAssembly_5', 1),
        Parameter('rvs_ProtMet_RuleAssembly_5', 1))

Rule('ProtMet_RuleAssembly_6',
        prot(name = 'crp', loc = 'cyt', met = 2, up = None, dw = 1) %
        met(name = 'CAMP', loc = 'cyt', prot = 2) %
        prot(name = 'crp', loc = 'cyt', met = None, up = 1, dw = None) +
        met(name = 'CAMP', loc = 'cyt', prot = None) |
        prot(name = 'crp', loc = 'cyt', met = 2, up = None, dw = 1) %
        met(name = 'CAMP', loc = 'cyt', prot = 2) %
        prot(name = 'crp', loc = 'cyt', met = 3, up = 1, dw = None) %
        met(name = 'CAMP', loc = 'cyt', prot = 3),
        Parameter('fwd_ProtMet_RuleAssembly_6', 1),
        Parameter('rvs_ProtMet_RuleAssembly_6', 1))

Rule('ProtMet_RuleAssembly_7',
        prot(name = 'lacI', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'lacI', loc = 'cyt', met = None, up = 1, dw = None) +
```

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```
        met(name = 'ALLOLACTOSE', loc = 'cyt', prot = None) |
        prot(name = 'lacI', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'lacI', loc = 'cyt', met = 2, up = 1, dw = None) %
        met(name = 'ALLOLACTOSE', loc = 'cyt', prot = 2),
        Parameter('fwd_ProtMet_RuleAssembly_7', 1),
        Parameter('rvs_ProtMet_RuleAssembly_7', 1))

Rule('ProtMet_RuleAssembly_8',
        prot(name = 'lacI', loc = 'cyt', met = 2, up = None, dw = 1) %
        met(name = 'ALLOLACTOSE', loc = 'cyt', prot = 2) %
        prot(name = 'lacI', loc = 'cyt', met = None, up = 1, dw = None) +
        met(name = 'ALLOLACTOSE', loc = 'cyt', prot = None) |
        prot(name = 'lacI', loc = 'cyt', met = 2, up = None, dw = 1) %
        met(name = 'ALLOLACTOSE', loc = 'cyt', prot = 2) %
        prot(name = 'lacI', loc = 'cyt', met = 3, up = 1, dw = None) %
        met(name = 'ALLOLACTOSE', loc = 'cyt', prot = 3),
        Parameter('fwd_ProtMet_RuleAssembly_8', 1),
        Parameter('rvs_ProtMet_RuleAssembly_8', 1))

Rule('ProtMet_RuleAssembly_9',
        prot(name = 'araG', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'araG', loc = 'cyt', met = None, up = 1, dw = None) +
        met(name = 'ATP', loc = 'cyt', prot = None) |
        prot(name = 'araG', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'araG', loc = 'cyt', met = 2, up = 1, dw = None) %
        met(name = 'ATP', loc = 'cyt', prot = 2),
        Parameter('fwd_ProtMet_RuleAssembly_9', 1),
        Parameter('rvs_ProtMet_RuleAssembly_9', 1))

Rule('ProtMet_RuleAssembly_10',
        prot(name = 'araC', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'araC', loc = 'cyt', met = None, up = 1, dw = None) +
        met(name = 'alpha_L_arabinopyranose', loc = 'cyt', prot = None) |
        prot(name = 'araC', loc = 'cyt', met = None, up = None, dw = 1) %
        prot(name = 'araC', loc = 'cyt', met = 2, up = 1, dw = None) %
        met(name = 'alpha_L_arabinopyranose', loc = 'cyt', prot = 2),
        Parameter('fwd_ProtMet_RuleAssembly_10', 1),
        Parameter('rvs_ProtMet_RuleAssembly_10', 1))

Rule('ProtMet_RuleAssembly_11',
        prot(name = 'araC', loc = 'cyt', met = 2, up = None, dw = 1) %
        met(name = 'alpha_L_arabinopyranose', loc = 'cyt', prot = 2) %
        prot(name = 'araC', loc = 'cyt', met = None, up = 1, dw = None) +
        met(name = 'alpha_L_arabinopyranose', loc = 'cyt', prot = None) |
        prot(name = 'araC', loc = 'cyt', met = 2, up = None, dw = 1) %
        met(name = 'alpha_L_arabinopyranose', loc = 'cyt', prot = 2) %
        prot(name = 'araC', loc = 'cyt', met = 3, up = 1, dw = None) %
        met(name = 'alpha_L_arabinopyranose', loc = 'cyt', prot = 3),
        Parameter('fwd_ProtMet_RuleAssembly_11', 1),
        Parameter('rvs_ProtMet_RuleAssembly_11', 1))
```

Note: **Reversibility of Rules**. Atlas writes reversible *Rules* for each reaction declared in the network file. The `Parameter('rvs_RuleName', 1))` must be set to zero to define an irreversible reaction.

Note: Uniqueness of Rule names. Atlas will write *Rules* with numbered names. Use only one file to model the many interactions the system has.

Note: Simulation. The model can be simulated only with the instantiation of `Monomers` and `Initials` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the necessary `Monomers` and `Initials` (including proteins and enzymatic complexes). Manually add the necessary `Monomers` and `Initials` for non-enzymatic proteins.

Plotting. The model can be observed only with the instantation of `Observables` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the all possible `Observables` for enzymatic proteins. Other observables for proteins should be added manually.

2.4 Transcription Factor-DNA Binding Site Interaction Networks

The transcription factor-DNA binding site network represents the physical interaction bewteen proteins and DNA. The network have two columns and for the former network, the first column lists using comma all components of a TF enclosed in brackets (optionally with small compounds) and in the second column declares the DNA binding site. Users should use the prefix "SMALL-" for small compounds and the prefix "BS-" to encode DNA binding sites using unique names. The second type of GRN shows in the first column the RNA polymerase holoenzyme complex (components in brackets) and in the second the promoter. Users should name promoters with the gene name followed by the suffix "-pro#" where # is an integer.

Examples:

```
SOURCE        TARGET
# araBAD and araC
[crp, SMALL-CAMP, crp, SMALL-CAMP]        BS-83-104
[crp, SMALL-CAMP, crp, SMALL-CAMP]        [BS-83-104, BS-araB-pro1]

araC        BS-35-51
araC        BS-56-72
araC        BS-109-125
araC        BS-130-146
araC        BS-267-283

[araC, BS-56-72]        [araC, BS-267-283, BS-araC-pro1]

[araC, SMALL-alpha-L-arabinopyranose]        BS-35-51
[araC, BS-56-72]        SMALL-alpha-L-arabinopyranose
[araC, BS-267-283]        SMALL-alpha-L-arabinopyranose

[araC, SMALL-alpha-L-arabinopyranose, BS-56-72]        [araC, SMALL-alpha-L-
↪arabinopyranose, BS-35-51, BS-araB-pro1]

# araFGH
[araC, SMALL-alpha-L-arabinopyranose]        BS-158-174
[araC, SMALL-alpha-L-arabinopyranose]        BS-137-153
[araC, SMALL-alpha-L-arabinopyranose]        BS-83-99
[araC, SMALL-alpha-L-arabinopyranose]        BS-62-78

[araC, SMALL-alpha-L-arabinopyranose, BS-83-99]        [araC, SMALL-alpha-L-
↪arabinopyranose, BS-62-78, BS-araF-pro1]
```

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```

# araE
[araC, SMALL-alpha-L-arabinopyranose]        BS-57-73
[araC, SMALL-alpha-L-arabinopyranose]        BS-36-52

[araC, SMALL-alpha-L-arabinopyranose, BS-57-73]        [araC, SMALL-alpha-L-
↪arabinopyranose, BS-36-52, BS-araE-pro1]
```

Finally, execute the "*Rules from tf-tfbs.ipynb*" to obtain the *Rules* to model the defined interaction network. The complete rule-based model can be found in the arabinose folder from the Network Biology Lab GitHub repository here.

```
# [crp, SMALL_CAMP, crp, SMALL_CAMP] interacts with BS_83_104
Rule('TranscriptionFactorMet_AssemblyRule_1',
        prot(name = 'crp', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'CAMP', prot = 3) %
        prot(name = 'crp', dna = None, met = 3, up = 1, dw = None) %
        met(name = 'CAMP', prot = 2) +
        dna(name = 'BS_83_104', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'crp', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'CAMP', prot = 3) %
        prot(name = 'crp', dna = 4, met = 3, up = 1, dw = None) %
        met(name = 'CAMP', prot = 2) %
        dna(name = 'BS_83_104', prot = 4, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_1', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_1', 0))

# [crp, SMALL_CAMP, crp, SMALL_CAMP] interacts with [BS_83_104, BS_araB_pro1]
Rule('TranscriptionFactorMet_AssemblyRule_2',
        prot(name = 'crp', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'CAMP', prot = 3) %
        prot(name = 'crp', dna = None, met = 3, up = 1, dw = None) %
        met(name = 'CAMP', prot = 2) +
        dna(name = 'BS_83_104', prot = None, free = 'True', up = WILD, dw = WILD) %
        dna(name = 'araB', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
↪WILD) |
        prot(name = 'crp', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'CAMP', prot = 3) %
        prot(name = 'crp', dna = 4, met = 3, up = 1, dw = None) %
        met(name = 'CAMP', prot = 2) %
        dna(name = 'BS_83_104', prot = 4, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araB', type = 'pro1', prot = None, free = 'False', up = WILD, dw␣
↪= WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_2', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_2', 0))

# araC interacts with BS_35_51
Rule('TranscriptionFactorMet_AssemblyRule_3',
        prot(name = 'araC', dna = None, met = None, up = None, dw = None) +
        dna(name = 'BS_35_51', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_35_51', prot = 1, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_3', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_3', 0))

# araC interacts with BS_56_72
```

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```
Rule('TranscriptionFactorMet_AssemblyRule_4',
        prot(name = 'araC', dna = None, met = None, up = None, dw = None) +
        dna(name = 'BS_56_72', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_56_72', prot = 1, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_4', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_4', 0))

# araC interacts with BS_109_125
Rule('TranscriptionFactorMet_AssemblyRule_5',
        prot(name = 'araC', dna = None, met = None, up = None, dw = None) +
        dna(name = 'BS_109_125', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_109_125', prot = 1, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_5', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_5', 0))

# araC interacts with BS_130_146
Rule('TranscriptionFactorMet_AssemblyRule_6',
        prot(name = 'araC', dna = None, met = None, up = None, dw = None) +
        dna(name = 'BS_130_146', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_130_146', prot = 1, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_6', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_6', 0))

# araC interacts with BS_267_283
Rule('TranscriptionFactorMet_AssemblyRule_7',
        prot(name = 'araC', dna = None, met = None, up = None, dw = None) +
        dna(name = 'BS_267_283', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_267_283', prot = 1, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_7', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_7', 0))

# [araC, BS_56_72] interacts with [araC, BS_267_283, BS_araC_pro1]
Rule('TranscriptionFactorMet_AssemblyRule_8',
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_56_72', prot = 1, free = 'False', up = WILD, dw = WILD) +
        prot(name = 'araC', dna = 2, met = None, up = None, dw = None) %
        dna(name = 'BS_267_283', prot = 2, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araC', type = 'pro1', prot = None, free = 'False', up = WILD, dw
↪= WILD) |
        prot(name = 'araC', dna = None, met = None, up = None, dw = 1) %
        dna(name = 'BS_56_72', prot = 2, free = 'False', up = WILD, dw = WILD) %
        prot(name = 'araC', dna = 2, met = None, up = 1, dw = None) %
        dna(name = 'BS_267_283', prot = None, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araC', type = 'pro1', prot = None, free = 'False', up = WILD, dw
↪= WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_8', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_8', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_35_51
Rule('TranscriptionFactorMet_AssemblyRule_9',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_35_51', prot = None, free = 'True', up = WILD, dw = WILD) |
```

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```
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_35_51', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_9', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_9', 0))

# [araC, BS_56_72] interacts with SMALL_alpha_L_arabinopyranose
Rule('TranscriptionFactorMet_AssemblyRule_10',
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_56_72', prot = 1, free = 'False', up = WILD, dw = WILD) +
        met(name = 'alpha_L_arabinopyranose', prot = None) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        dna(name = 'BS_56_72', prot = 2, free = 'False', up = WILD, dw = WILD) %
        met(name = 'alpha_L_arabinopyranose', prot = 1),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_10', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_10', 0))

# [araC, BS_267_283] interacts with SMALL_alpha_L_arabinopyranose
Rule('TranscriptionFactorMet_AssemblyRule_11',
        prot(name = 'araC', dna = 1, met = None, up = None, dw = None) %
        dna(name = 'BS_267_283', prot = 1, free = 'False', up = WILD, dw = WILD) +
        met(name = 'alpha_L_arabinopyranose', prot = None) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        dna(name = 'BS_267_283', prot = 2, free = 'False', up = WILD, dw = WILD) %
        met(name = 'alpha_L_arabinopyranose', prot = 1),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_11', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_11', 0))

# [araC, SMALL_alpha_L_arabinopyranose, BS_56_72] interacts with [araC, SMALL_alpha_L_
↪arabinopyranose, BS_35_51, BS_araB_pro1]
Rule('TranscriptionFactorMet_AssemblyRule_12',
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_56_72', prot = 2, free = 'False', up = WILD, dw = WILD) +
        prot(name = 'araC', dna = 4, met = 3, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 3) %
        dna(name = 'BS_35_51', prot = 4, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araB', type = 'pro1', prot = None, free = 'False', up = WILD, dw␣
↪= WILD) |
        prot(name = 'araC', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'alpha_L_arabinopyranose', prot = 3) %
        dna(name = 'BS_56_72', prot = 4, free = 'False', up = WILD, dw = WILD) %
        prot(name = 'araC', dna = 4, met = 3, up = 1, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 2) %
        dna(name = 'BS_35_51', prot = None, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araB', type = 'pro1', prot = None, free = 'False', up = WILD, dw␣
↪= WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_12', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_12', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_158_174
Rule('TranscriptionFactorMet_AssemblyRule_13',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_158_174', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
```

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```
        dna(name = 'BS_158_174', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_13', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_13', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_137_153
Rule('TranscriptionFactorMet_AssemblyRule_14',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_137_153', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_137_153', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_14', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_14', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_83_99
Rule('TranscriptionFactorMet_AssemblyRule_15',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_83_99', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_83_99', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_15', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_15', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_62_78
Rule('TranscriptionFactorMet_AssemblyRule_16',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_62_78', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_62_78', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_16', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_16', 0))

# [araC, SMALL_alpha_L_arabinopyranose, BS_83_99] interacts with [araC, SMALL_alpha_L_
↪arabinopyranose, BS_62_78, BS_araF_pro1]
Rule('TranscriptionFactorMet_AssemblyRule_17',
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_83_99', prot = 2, free = 'False', up = WILD, dw = WILD) +
        prot(name = 'araC', dna = 4, met = 3, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 3) %
        dna(name = 'BS_62_78', prot = 4, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araF', type = 'pro1', prot = None, free = 'False', up = WILD, dw_
↪= WILD) |
        prot(name = 'araC', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'alpha_L_arabinopyranose', prot = 3) %
        dna(name = 'BS_83_99', prot = 4, free = 'False', up = WILD, dw = WILD) %
        prot(name = 'araC', dna = 4, met = 3, up = 1, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 2) %
        dna(name = 'BS_62_78', prot = None, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araF', type = 'pro1', prot = None, free = 'False', up = WILD, dw_
↪= WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_17', 0),
```

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```
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_17', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_57_73
Rule('TranscriptionFactorMet_AssemblyRule_18',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_57_73', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_57_73', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_18', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_18', 0))

# [araC, SMALL_alpha_L_arabinopyranose] interacts with BS_36_52
Rule('TranscriptionFactorMet_AssemblyRule_19',
        prot(name = 'araC', dna = None, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) +
        dna(name = 'BS_36_52', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_36_52', prot = 2, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_19', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_19', 0))

# [araC, SMALL_alpha_L_arabinopyranose, BS_57_73] interacts with [araC, SMALL_alpha_L_
↪arabinopyranose, BS_36_52, BS_araE_pro1]
Rule('TranscriptionFactorMet_AssemblyRule_20',
        prot(name = 'araC', dna = 2, met = 1, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 1) %
        dna(name = 'BS_57_73', prot = 2, free = 'False', up = WILD, dw = WILD) +
        prot(name = 'araC', dna = 4, met = 3, up = None, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 3) %
        dna(name = 'BS_36_52', prot = 4, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araE', type = 'pro1', prot = None, free = 'False', up = WILD, dw␣
↪= WILD) |
        prot(name = 'araC', dna = None, met = 2, up = None, dw = 1) %
        met(name = 'alpha_L_arabinopyranose', prot = 3) %
        dna(name = 'BS_57_73', prot = 4, free = 'False', up = WILD, dw = WILD) %
        prot(name = 'araC', dna = 4, met = 3, up = 1, dw = None) %
        met(name = 'alpha_L_arabinopyranose', prot = 2) %
        dna(name = 'BS_36_52', prot = None, free = 'False', up = WILD, dw = WILD) %
        dna(name = 'araE', type = 'pro1', prot = None, free = 'False', up = WILD, dw␣
↪= WILD),
        Parameter('fwd_TranscriptionFactorMet_AssemblyRule_20', 0),
        Parameter('rvs_TranscriptionFactorMet_AssemblyRule_20', 0))
```

Note: Reversibility of reactions. Atlas writes dead *Rules* for each reaction declared in the network file. The `Parameter('fwd_ReactionName', 0))` must be set to non-zero to activate the rule and `Parameter('rvs_ReactionName', 0))` must be set to non-zero to define a reversible reaction.

Note: Simulation. The model can be simulated only with the instantiation of `Monomers` and `Initials` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the necessary `Monomers` and `Initials` (including proteins and enzymatic complexes).

Plotting. The model can be observed only with the instantation of `Observables` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the all possible `Observables` for metabolites.

2.5 Sigma Factor-Promoter Interaction Networks

The Sigma Factor-Promoter network have two columns and for the former network, the first column lists using comma all components of a TF enclosed in brackets (optionally with small compounds) and in the second column declares the DNA binding site. Users should use the prefix "SMALL-" for small compounds and the prefix "BS-" to encode DNA binding sites using unique names. The second type of GRN shows in the first column the RNA polymerase holoenzyme complex (components in brackets) and in the second the promoter. Users should name promoters with the gene name followed by the suffix "-pro#" where # is an integer.

Examples:

```
SOURCE        TARGET
# Docking to promoters
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoA-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoB-pro1
# [rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoC-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoD-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoE-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoH-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoN-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-rpoS-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-fliA-pro1
[rpoA, rpoA, rpoB, rpoC, rpoD]        BS-fecI-pro1

[rpoA, rpoA, rpoB, rpoC, rpoE]        BS-rpoD-pro1
[rpoA, rpoA, rpoB, rpoC, rpoE]        BS-rpoE-pro1
[rpoA, rpoA, rpoB, rpoC, rpoE]        BS-rpoH-pro1
[rpoA, rpoA, rpoB, rpoC, rpoE]        BS-rpoN-pro1

[rpoA, rpoA, rpoB, rpoC, rpoH]        BS-rpoA-pro1
[rpoA, rpoA, rpoB, rpoC, rpoH]        BS-rpoD-pro1

[rpoA, rpoA, rpoB, rpoC, rpoN]        BS-rpoA-pro1
[rpoA, rpoA, rpoB, rpoC, rpoN]        BS-rpoD-pro1
[rpoA, rpoA, rpoB, rpoC, rpoN]        BS-rpoH-pro1

[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-fecI-pro1
[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoA-pro1
[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoB-pro1
# [rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoC-pro1
[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoD-pro1
[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoE-pro1
[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoH-pro1
[rpoA, rpoA, rpoB, rpoC, rpoS]        BS-rpoN-pro1

[rpoA, rpoA, rpoB, rpoC, fliA]        BS-rpoD-pro1
[rpoA, rpoA, rpoB, rpoC, fliA]        BS-rpoN-pro1
[rpoA, rpoA, rpoB, rpoC, fliA]        BS-fliA-pro1
```

Finally, execute the "*Rules from SigmaFactors x Architecture.ipynb*" to obtain the *Rules* to model the defined interaction network. The complete rule-based model can be found in the sigma folder from the Network Biology Lab GitHub

repository here.

```
# [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoA_pro1
Rule('docking_1_rpoA_pro1',
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
        dna(name = 'rpoA', type = 'pro1', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
        dna(name = 'rpoA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_docking_1_rpoA_pro1', 0),
        Parameter('rvs_docking_1_rpoA_pro1', 0))

# [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoB_pro1
Rule('docking_2_rpoB_pro1',
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
        dna(name = 'rpoB', type = 'pro1', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
        dna(name = 'rpoB', type = 'pro1', prot = 5, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_docking_2_rpoB_pro1', 0),
        Parameter('rvs_docking_2_rpoB_pro1', 0))

# [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoD_pro1
Rule('docking_3_rpoD_pro1',
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
        dna(name = 'rpoD', type = 'pro1', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
        dna(name = 'rpoD', type = 'pro1', prot = 5, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_docking_3_rpoD_pro1', 0),
        Parameter('rvs_docking_3_rpoD_pro1', 0))
```

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```
51
52  # [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoE_pro1
53  Rule('docking_4_rpoE_pro1',
54          prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
55          prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
56          prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
57          prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
58          prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
59          dna(name = 'rpoE', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
60          prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
61          prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
62          prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
63          prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
64          prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
65          dna(name = 'rpoE', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
66          Parameter('fwd_docking_4_rpoE_pro1', 0),
67          Parameter('rvs_docking_4_rpoE_pro1', 0))
68
69  # [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoH_pro1
70  Rule('docking_5_rpoH_pro1',
71          prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
72          prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
73          prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
74          prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
75          prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
76          dna(name = 'rpoH', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
77          prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
78          prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
79          prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
80          prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
81          prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
82          dna(name = 'rpoH', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
83          Parameter('fwd_docking_5_rpoH_pro1', 0),
84          Parameter('rvs_docking_5_rpoH_pro1', 0))
85
86  # [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoN_pro1
87  Rule('docking_6_rpoN_pro1',
88          prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
89          prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
90          prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
91          prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
92          prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
93          dna(name = 'rpoN', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
94          prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
95          prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
96          prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
97          prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
98          prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
99          dna(name = 'rpoN', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
100         Parameter('fwd_docking_6_rpoN_pro1', 0),
101         Parameter('rvs_docking_6_rpoN_pro1', 0))
```

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```
102
103 # [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoS_pro1
104 Rule('docking_7_rpoS_pro1',
105         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
106         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
107         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
108         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
109         prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
110         dna(name = 'rpoS', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
111         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
112         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
113         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
114         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
115         prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
116         dna(name = 'rpoS', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
117         Parameter('fwd_docking_7_rpoS_pro1', 0),
118         Parameter('rvs_docking_7_rpoS_pro1', 0))
119
120 # [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_fliA_pro1
121 Rule('docking_8_fliA_pro1',
122         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
123         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
124         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
125         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
126         prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
127         dna(name = 'fliA', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
128         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
129         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
130         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
131         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
132         prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
133         dna(name = 'fliA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
134         Parameter('fwd_docking_8_fliA_pro1', 0),
135         Parameter('rvs_docking_8_fliA_pro1', 0))
136
137 # [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_fecI_pro1
138 Rule('docking_9_fecI_pro1',
139         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
140         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
141         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
142         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
143         prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
144         dna(name = 'fecI', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
145         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
146         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
147         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
148         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
149         prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
150         dna(name = 'fecI', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
151         Parameter('fwd_docking_9_fecI_pro1', 0),
152         Parameter('rvs_docking_9_fecI_pro1', 0))
```

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```
153
154 # [rpoA, rpoA, rpoB, rpoC, rpoE] interacts with BS_rpoD_pro1
155 Rule('docking_10_rpoD_pro1',
156         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
157         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
158         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
159         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
160         prot(name = 'rpoE', dna = None, met = None, up = 4, dw = None) +
161         dna(name = 'rpoD', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
162         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
163         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
164         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
165         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
166         prot(name = 'rpoE', dna = 5, met = None, up = 4, dw = None) %
167         dna(name = 'rpoD', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
168         Parameter('fwd_docking_10_rpoD_pro1', 0),
169         Parameter('rvs_docking_10_rpoD_pro1', 0))
170
171 # [rpoA, rpoA, rpoB, rpoC, rpoE] interacts with BS_rpoE_pro1
172 Rule('docking_11_rpoE_pro1',
173         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
174         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
175         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
176         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
177         prot(name = 'rpoE', dna = None, met = None, up = 4, dw = None) +
178         dna(name = 'rpoE', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
179         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
180         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
181         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
182         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
183         prot(name = 'rpoE', dna = 5, met = None, up = 4, dw = None) %
184         dna(name = 'rpoE', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
185         Parameter('fwd_docking_11_rpoE_pro1', 0),
186         Parameter('rvs_docking_11_rpoE_pro1', 0))
187
188 # [rpoA, rpoA, rpoB, rpoC, rpoE] interacts with BS_rpoH_pro1
189 Rule('docking_12_rpoH_pro1',
190         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
191         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
192         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
193         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
194         prot(name = 'rpoE', dna = None, met = None, up = 4, dw = None) +
195         dna(name = 'rpoH', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
196         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
197         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
198         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
199         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
200         prot(name = 'rpoE', dna = 5, met = None, up = 4, dw = None) %
201         dna(name = 'rpoH', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
202         Parameter('fwd_docking_12_rpoH_pro1', 0),
203         Parameter('rvs_docking_12_rpoH_pro1', 0))
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204
205 # [rpoA, rpoA, rpoB, rpoC, rpoE] interacts with BS_rpoN_pro1
206 Rule('docking_13_rpoN_pro1',
207         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
208         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
209         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
210         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
211         prot(name = 'rpoE', dna = None, met = None, up = 4, dw = None) +
212         dna(name = 'rpoN', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
213         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
214         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
215         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
216         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
217         prot(name = 'rpoE', dna = 5, met = None, up = 4, dw = None) %
218         dna(name = 'rpoN', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
219         Parameter('fwd_docking_13_rpoN_pro1', 0),
220         Parameter('rvs_docking_13_rpoN_pro1', 0))
221
222 # [rpoA, rpoA, rpoB, rpoC, rpoH] interacts with BS_rpoA_pro1
223 Rule('docking_14_rpoA_pro1',
224         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
225         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
226         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
227         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
228         prot(name = 'rpoH', dna = None, met = None, up = 4, dw = None) +
229         dna(name = 'rpoA', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
230         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
231         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
232         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
233         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
234         prot(name = 'rpoH', dna = 5, met = None, up = 4, dw = None) %
235         dna(name = 'rpoA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
236         Parameter('fwd_docking_14_rpoA_pro1', 0),
237         Parameter('rvs_docking_14_rpoA_pro1', 0))
238
239 # [rpoA, rpoA, rpoB, rpoC, rpoH] interacts with BS_rpoD_pro1
240 Rule('docking_15_rpoD_pro1',
241         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
242         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
243         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
244         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
245         prot(name = 'rpoH', dna = None, met = None, up = 4, dw = None) +
246         dna(name = 'rpoD', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
247         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
248         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
249         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
250         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
251         prot(name = 'rpoH', dna = 5, met = None, up = 4, dw = None) %
252         dna(name = 'rpoD', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
253         Parameter('fwd_docking_15_rpoD_pro1', 0),
254         Parameter('rvs_docking_15_rpoD_pro1', 0))
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255
256 # [rpoA, rpoA, rpoB, rpoC, rpoN] interacts with BS_rpoA_pro1
257 Rule('docking_16_rpoA_pro1',
258         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
259         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
260         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
261         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
262         prot(name = 'rpoN', dna = None, met = None, up = 4, dw = None) +
263         dna(name = 'rpoA', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
264         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
265         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
266         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
267         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
268         prot(name = 'rpoN', dna = 5, met = None, up = 4, dw = None) %
269         dna(name = 'rpoA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
270         Parameter('fwd_docking_16_rpoA_pro1', 0),
271         Parameter('rvs_docking_16_rpoA_pro1', 0))
272
273 # [rpoA, rpoA, rpoB, rpoC, rpoN] interacts with BS_rpoD_pro1
274 Rule('docking_17_rpoD_pro1',
275         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
276         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
277         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
278         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
279         prot(name = 'rpoN', dna = None, met = None, up = 4, dw = None) +
280         dna(name = 'rpoD', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
281         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
282         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
283         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
284         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
285         prot(name = 'rpoN', dna = 5, met = None, up = 4, dw = None) %
286         dna(name = 'rpoD', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
287         Parameter('fwd_docking_17_rpoD_pro1', 0),
288         Parameter('rvs_docking_17_rpoD_pro1', 0))
289
290 # [rpoA, rpoA, rpoB, rpoC, rpoN] interacts with BS_rpoH_pro1
291 Rule('docking_18_rpoH_pro1',
292         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
293         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
294         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
295         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
296         prot(name = 'rpoN', dna = None, met = None, up = 4, dw = None) +
297         dna(name = 'rpoH', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
298         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
299         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
300         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
301         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
302         prot(name = 'rpoN', dna = 5, met = None, up = 4, dw = None) %
303         dna(name = 'rpoH', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
304         Parameter('fwd_docking_18_rpoH_pro1', 0),
305         Parameter('rvs_docking_18_rpoH_pro1', 0))
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306
307 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_fecI_pro1
308 Rule('docking_19_fecI_pro1',
309         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
310         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
311         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
312         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
313         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
314         dna(name = 'fecI', type = 'pro1', prot = None, free = 'True', up = WILD, dw =
    ↪WILD) |
315         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
316         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
317         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
318         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
319         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
320         dna(name = 'fecI', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =
    ↪WILD),
321         Parameter('fwd_docking_19_fecI_pro1', 0),
322         Parameter('rvs_docking_19_fecI_pro1', 0))
323
324 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_rpoA_pro1
325 Rule('docking_20_rpoA_pro1',
326         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
327         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
328         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
329         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
330         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
331         dna(name = 'rpoA', type = 'pro1', prot = None, free = 'True', up = WILD, dw =
    ↪WILD) |
332         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
333         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
334         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
335         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
336         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
337         dna(name = 'rpoA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =
    ↪WILD),
338         Parameter('fwd_docking_20_rpoA_pro1', 0),
339         Parameter('rvs_docking_20_rpoA_pro1', 0))
340
341 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_rpoB_pro1
342 Rule('docking_21_rpoB_pro1',
343         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
344         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
345         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
346         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
347         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
348         dna(name = 'rpoB', type = 'pro1', prot = None, free = 'True', up = WILD, dw =
    ↪WILD) |
349         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
350         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
351         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
352         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
353         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
354         dna(name = 'rpoB', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =
    ↪WILD),
355         Parameter('fwd_docking_21_rpoB_pro1', 0),
356         Parameter('rvs_docking_21_rpoB_pro1', 0))
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357
358 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_rpoD_pro1
359 Rule('docking_22_rpoD_pro1',
360         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
361         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
362         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
363         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
364         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
365         dna(name = 'rpoD', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
366         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
367         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
368         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
369         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
370         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
371         dna(name = 'rpoD', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
372         Parameter('fwd_docking_22_rpoD_pro1', 0),
373         Parameter('rvs_docking_22_rpoD_pro1', 0))
374
375 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_rpoE_pro1
376 Rule('docking_23_rpoE_pro1',
377         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
378         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
379         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
380         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
381         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
382         dna(name = 'rpoE', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
383         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
384         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
385         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
386         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
387         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
388         dna(name = 'rpoE', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
389         Parameter('fwd_docking_23_rpoE_pro1', 0),
390         Parameter('rvs_docking_23_rpoE_pro1', 0))
391
392 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_rpoH_pro1
393 Rule('docking_24_rpoH_pro1',
394         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
395         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
396         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
397         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
398         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
399         dna(name = 'rpoH', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
400         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
401         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
402         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
403         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
404         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
405         dna(name = 'rpoH', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
406         Parameter('fwd_docking_24_rpoH_pro1', 0),
407         Parameter('rvs_docking_24_rpoH_pro1', 0))
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408
409 # [rpoA, rpoA, rpoB, rpoC, rpoS] interacts with BS_rpoN_pro1
410 Rule('docking_25_rpoN_pro1',
411         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
412         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
413         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
414         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
415         prot(name = 'rpoS', dna = None, met = None, up = 4, dw = None) +
416         dna(name = 'rpoN', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
417         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
418         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
419         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
420         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
421         prot(name = 'rpoS', dna = 5, met = None, up = 4, dw = None) %
422         dna(name = 'rpoN', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
423         Parameter('fwd_docking_25_rpoN_pro1', 0),
424         Parameter('rvs_docking_25_rpoN_pro1', 0))
425
426 # [rpoA, rpoA, rpoB, rpoC, fliA] interacts with BS_rpoD_pro1
427 Rule('docking_26_rpoD_pro1',
428         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
429         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
430         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
431         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
432         prot(name = 'fliA', dna = None, met = None, up = 4, dw = None) +
433         dna(name = 'rpoD', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
434         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
435         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
436         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
437         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
438         prot(name = 'fliA', dna = 5, met = None, up = 4, dw = None) %
439         dna(name = 'rpoD', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
440         Parameter('fwd_docking_26_rpoD_pro1', 0),
441         Parameter('rvs_docking_26_rpoD_pro1', 0))
442
443 # [rpoA, rpoA, rpoB, rpoC, fliA] interacts with BS_rpoN_pro1
444 Rule('docking_27_rpoN_pro1',
445         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
446         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
447         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
448         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
449         prot(name = 'fliA', dna = None, met = None, up = 4, dw = None) +
450         dna(name = 'rpoN', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
    ↪WILD) |
451         prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
452         prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
453         prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
454         prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
455         prot(name = 'fliA', dna = 5, met = None, up = 4, dw = None) %
456         dna(name = 'rpoN', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
    ↪WILD),
457         Parameter('fwd_docking_27_rpoN_pro1', 0),
458         Parameter('rvs_docking_27_rpoN_pro1', 0))
```

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```

# [rpoA, rpoA, rpoB, rpoC, fliA] interacts with BS_fliA_pro1
Rule('docking_28_fliA_pro1',
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'fliA', dna = None, met = None, up = 4, dw = None) +
        dna(name = 'fliA', type = 'pro1', prot = None, free = 'True', up = WILD, dw = WILD) |
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'fliA', dna = 5, met = None, up = 4, dw = None) %
        dna(name = 'fliA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw = WILD),
        Parameter('fwd_docking_28_fliA_pro1', 0),
        Parameter('rvs_docking_28_fliA_pro1', 0))
```

Note: **Reversibility of reactions**. Atlas writes dead *Rules* for each reaction declared in the network file. The `Parameter('fwd_ReactionName', 0))` must be set to non-zero to activate the rule and `Parameter('rvs_ReactionName', 0))` must be set to non-zero to define a reversible reaction.

Note: **Simulation**. The model can be simulated only with the instantiation of `Monomers` and `Initials` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the necessary `Monomers` and `Initials` (including proteins and enzymatic complexes).

Plotting. The model can be observed only with the instantation of `Observables` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the all possible `Observables` for metabolites.

2.6 Genome Graphs

Metabolic networks have four columns. The first declares a unique name for the enzyme or enzymatic complex; the second declares a unique name for the reaction; the third column lists using comma unique names for substrates; and the last row list using comma unique names for products. To declare metabolites located at the periplasm or extracellular compartments, the user should employ the prefix "PER-" and "EX-", respectively. Use *spontaneous* for non-enzymatic reactions.

Examples:

```
SOURCE        TARGET
araB-pro1        araB-rbs
araB-rbs        araB-cds
araB-cds        araA-rbs
araA-rbs        araA-cds
araA-cds        araD-rbs
araD-rbs        araD-cds
araD-cds        araD-ter1
```

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```
araC-pro1        araC-BS-56-72
araC-BS-56-72        araC-rbs
araC-rbs         araC-cds
araC-cds         araC-ter1

araE-pro1        araE-rbs
araE-rbs         araE-cds
araE-cds         araE-ter1

araF-pro1        araF-rbs
araF-rbs         araF-cds
araF-cds         araG-rbs
araG-rbs         araG-cds
araG-cds         araH-rbs
araH-rbs         araH-cds
araH-cds         araH-ter1
```

OR

```
SOURCE         TARGET
rpoA-pro1        rpoA-rbs
rpoA-rbs         rpoA-cds
rpoA-cds         rpoA-ter1

rpoB-pro1        rpoB-rbs
rpoB-rbs         rpoB-cds
rpoB-cds         rpoC-rbs
rpoC-rbs         rpoC-cds
rpoC-cds         rpoC-ter1

rpoD-pro1        rpoD-rbs
rpoD-rbs         rpoD-cds
rpoD-cds         rpoD-ter1

rpoE-pro1        rpoE-rbs
rpoE-rbs         rpoE-cds
rpoE-cds         rpoE-ter1

rpoH-pro1        rpoH-rbs
rpoH-rbs         rpoH-cds
rpoH-cds         rpoH-ter1

rpoN-pro1        rpoN-rbs
rpoN-rbs         rpoN-cds
rpoN-cds         rpoN-ter1

rpoS-pro1        rpoS-rbs
rpoS-rbs         rpoS-cds
rpoS-cds         rpoS-ter1

fliA-pro1        fliA-rbs
fliA-rbs         fliA-cds
fliA-cds         fliA-ter1

fecI-pro1        fecI-rbs
fecI-rbs         fecI-cds
```

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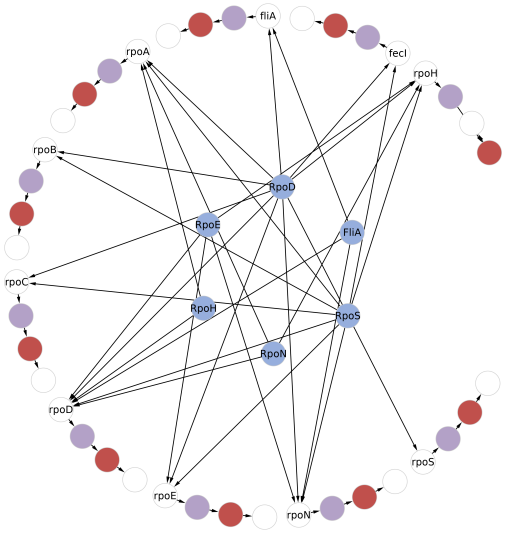
```
fecI-cds        fecI-ter1
```

Note: Visualization in Cytoscape. Colors and arrows remains to the user for customization. The network could be complemented with a description of sigma factor specifity for promoter, as the following network



Finally, execute the "*Rules from metabolic network.ipynb*" to obtain the *Rules* to model the defined network. If using a Sigma Factor-Promoter Interaction Network, the user could use "*Rules from SigmaFactors x Architecture*" to obtain the *Rules* to model both network at once. The complete rule-based model can be found in the arabinose folder (1st example) and in the sigma folder (2nd example) from the Network Biology Lab GitHub repository here.

Note: Kappa BioBrick Framework. The *Rules* for transcription and translation come from the work of Stewart and Wilson-Kanamori (See more here). A "pure" genome graph uses the originally defined rules, while a genome graph + sigma factor specifity uses a modified *rules* to model the release of the sigma factor from the RNA Polymerase at the transcription initiation. Please note the explicit modeling of the RNA Polymerase complex in the second example.

```
Rule('docking_araB_pro1',
        cplx(name = 'RNAP', dna = None) + dna(name = 'araB', type = 'pro1', prot =␣
↪None, free = 'True') |
        cplx(name = 'RNAP', dna = 1) % dna(name = 'araB', type = 'pro1', prot = 1,␣
↪free = 'False'),
        Parameter('fwd_docking_araB_pro1', 1), Parameter('rvs_docking_araB_pro1', 1))
```

OR

```
# [rpoA, rpoA, rpoB, rpoC, rpoD] interacts with BS_rpoA_pro1
Rule('docking_1_rpoA_pro1',
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = None, met = None, up = 4, dw = None) +
        dna(name = 'rpoA', type = 'pro1', prot = None, free = 'True', up = WILD, dw =␣
↪WILD) |
        prot(name = 'rpoA', dna = None, met = None, up = None, dw = 1) %
```

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```
        prot(name = 'rpoA', dna = None, met = None, up = 1, dw = 2) %
        prot(name = 'rpoB', dna = None, met = None, up = 2, dw = 3) %
        prot(name = 'rpoC', dna = None, met = None, up = 3, dw = 4) %
        prot(name = 'rpoD', dna = 5, met = None, up = 4, dw = None) %
        dna(name = 'rpoA', type = 'pro1', prot = 5, free = 'False', up = WILD, dw =␣
↪WILD),
        Parameter('fwd_docking_1_rpoA_rbs', 1),
        Parameter('rvs_docking_1_rpoA_pro1', 0))
```

Note: Reversibility of reactions. Atlas writes irreversible *Rules* for each interaction between the RNA Polymerase and a promoter. The `Parameter('rvs_ReactionName', 0))` must be set to non-zero to define a reversible reaction. The remaining *Rules* are irreversible without a way to define reversible reactions.

Note: Simulation. The model can be simulated only with the instantiation of `Monomers` and `Initials` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the necessary `Monomers` and `Initials` (including proteins and enzymatic complexes). For initial genes, please refer to the following example:

Plotting. The model can be observed only with the instantation of `Observables` (More here). Run *Monomer+Initials+Observables from metabolic network.ipynb* to obtain automatically the all possible `Observables` for metabolites.

CHAPTER

THREE

SIMULATION

Simulation could be done within the PySB python package (See more at PySB documentation) . Here is the relevant code that able the simulation of any PySB model, albeit PySB exports the model, calls the simulator, and imports the results under the hood. See *Plotting* for a simple example on how to plot simulation results.

```
from numpy import linspace
from pysb.bng import generate_network, generate_equations
from pysb.simulator import ScipyOdeSimulator, BngSimulator, KappaSimulator

# modify accordingly
from pysb.pathfinder import set_path
set_path('bng', '/opt/git-repositories/bionetgen.RuleWorld/bng2/')
set_path('kasim', '/opt/git-repositories/KaSim4.Kappa-Dev/')

## for network-based simulations:
## ScipyOdeSimulator and BngSimulator ode and ssa methods
# generate_network(model)
# generate_equations(model)

## set the number of stochastic simulations
runs = 100
# data1 = ScipyOdeSimulator(model, linspace(0, 100, 200)).run().dataframe
# data1 = BngSimulator(model, linspace(0, 200, 201)).run(method = 'ode').dataframe
# data2 = BngSimulator(model, linspace(0, 200, 201)).run(method = 'ssa', n_runs =
↪runs).dataframe
# data2 = BngSimulator(model, linspace(0, 200, 201)).run(method = 'nf', n_runs =
↪runs).dataframe
data2 = KappaSimulator(model, linspace(0, 100, 101)).run(n_runs = runs).dataframe

## process simulations
data = []
for i in range(0, runs):
        data.append(data2.xs(i))

avrg = 0
for i in range(0, runs):
        avrg += data[i]
avrg = avrg / runs

stdv = 0
for i in range(0, runs):
        stdv += (data[i] - avrg)**2
stdv = (stdv / (runs-1))**0.5
```

Note: Please follow the instructions at BioNetGen and at KaSim documentations to install the stochactic simulators. For network-based simulations (Ordinary Differential Equations and Gillespie`s algorithm), BioNetGen is required to perform the network generation. Change the corresponding paths (lines 7-8) to match the parent folder for the BNG2.pl or KaSim executable.

CHAPTER

FOUR

PLOTTING

PySB could inform the results of a simulation to dataframes (See *Simulation*) and visualization of results could be done with matplotlib or seaborn even (See more here). To access the data, the dataframes columns reproduce the names of the `Observables`. The following example could be adapted to show the dynamics of any `Observable`.

Note: Importantly, PySB allows the inspection of the model to find which `Monomers` (and complexes of monomers) exists in the model, but as the simulation is network-free, the possible formed complexes are up to the user concern.

Note: Atlas produces automatically `Observables` for metabolites, and other components and complexes could also be observed and plotted, but their declaration in the model is entirely up to the user.

```
fig, ax = plt.subplots(1, 2, figsize = (4*2, 3*1), dpi = 100)

# ax[0].plot(data1.index, data1['obs_alpha_L_arabinopyranose_cyt'], label = '__
↪NOLABEL__', color = palette[0])
# ax[0].plot(data1.index, data1['obs_ATP_cyt'], label = '__NOLABEL__', color =␣
↪palette[3])
ax[0].fill_between(avrg.index,
        avrg['obs_alpha_L_arabinopyranose_cyt'] + stdv['obs_alpha_L_arabinopyranose_
↪cyt'],
        avrg['obs_alpha_L_arabinopyranose_cyt'] - stdv['obs_alpha_L_arabinopyranose_
↪cyt'],
        label = r'$\alpha$-arabinopyranose', **{'color' : palette[0], 'alpha' : 0.5})
ax[0].fill_between(avrg.index,
        avrg['obs_ATP_cyt'] + stdv['obs_ATP_cyt'],
        avrg['obs_ATP_cyt'] - stdv['obs_ATP_cyt'],
        label = r'ATP', **{'color' : palette[3], 'alpha' : 0.5})

# ax[1].plot(data1.index, data1['obs_PROTON_cyt'], label = '__NOLABEL__', color =␣
↪palette[0])
# ax[1].plot(data1.index, data1['obs_XYLULOSE_5_PHOSPHATE_cyt'], label = '__NOLABEL__
↪', color = palette[3])
ax[1].fill_between(avrg.index,
        avrg['obs_PROTON_cyt'] + stdv['obs_PROTON_cyt'],
        avrg['obs_PROTON_cyt'] - stdv['obs_PROTON_cyt'],
        label = r'H$^+$', **{'color' : palette[0], 'alpha' : 0.5})
ax[1].fill_between(avrg.index,
        avrg['obs_WATER_cyt'] + stdv['obs_WATER_cyt'],
        avrg['obs_WATER_cyt'] - stdv['obs_WATER_cyt'],
        label = 'WATER', **{'color' : palette[1], 'alpha' : 0.5})
ax[1].fill_between(avrg.index,
```

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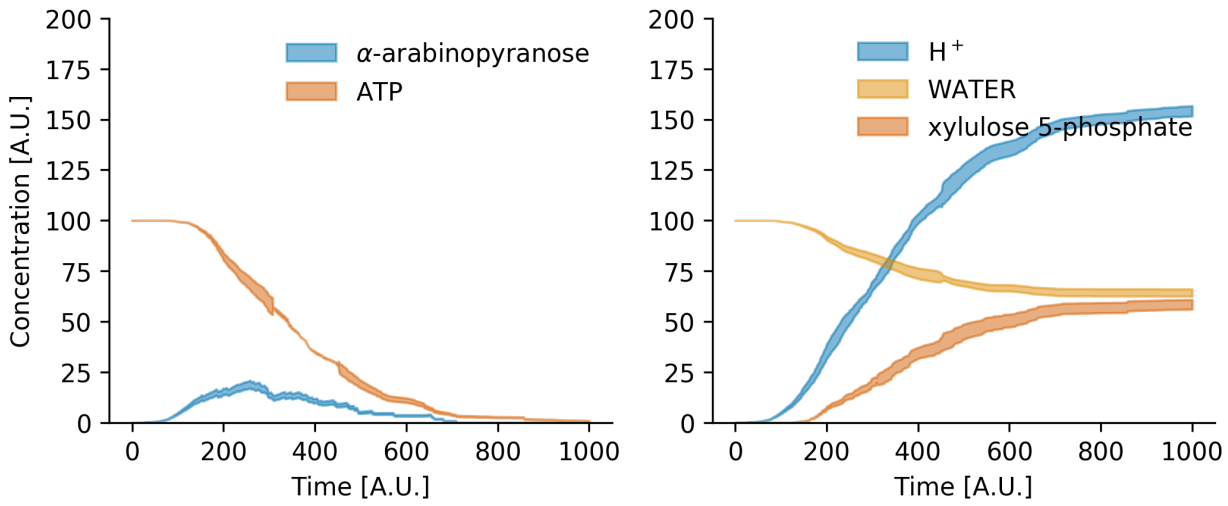
```
        avrg['obs_XYLULOSE_5_PHOSPHATE_cyt'] + stdv['obs_XYLULOSE_5_PHOSPHATE_cyt'],
        avrg['obs_XYLULOSE_5_PHOSPHATE_cyt'] - stdv['obs_XYLULOSE_5_PHOSPHATE_cyt'],
        label = r'xylulose 5-phosphate', **{'color' : palette[3], 'alpha' : 0.5})

ax[0].set_xlabel('Time [A.U.]')
ax[0].set_ylabel('Concentration [A.U.]')
# ax[0].set_xlim(left = 0, right = 100)
ax[0].set_ylim(bottom = 0, top = 200)

ax[1].set_xlabel('Time [A.U.]')
# ax[1].set_xlim(left = 0, right = 100)
ax[1].set_ylim(bottom = 0, top = 200)

ax[0].legend(frameon = False)
ax[1].legend(frameon = False)

seaborn.despine()
plt.savefig('Fig_Arabinose.png', format = 'png', bbox_inches = 'tight', dpi = 350)
# for publication
# plt.savefig('Fig_Arabinose.pdf', format = 'pdf', bbox_inches = 'tight', dpi = 350)

plt.show()
```

And the results is



Note: See the Arabinose Model to inspect the rules and reproduce (at some extent because of stochasticity) the plot showed in this Manual.

CHAPTER

FIVE

EXPORT TO

The PySB python package could export to different languages (See more here). Use the following code to export to BioNetGen and *kappa* languages, putting the code at the end of the model.

```
from pysb.export import export
with open('model.kappa', 'w') as outfile:
        outfile.write(export(model, 'kappa'))
with open('model.bngl', 'w') as outfile:
        outfile.write(export(model, 'bngl'))
```

Note: In the case of matlab, mathematica, and stochkit, PySB requires to expand the rules to determine all mass-balances to write ODE-based models, a proccess call network generation and could take excessive time to finish.

CHAPTER

SIX

INDICES AND TABLES

- genindex
- modindex
- search