

# Vesicle traffic system and constraints.

## 1 Formula variables

Basic notation for the formula we are trying to generate.

1.  $\text{edge} = e(i,j,q)$  There is an  $q$ th edge between node  $i$  and  $j$ .
2.  $\text{dump} = d(i,j,q)$  drop edge  $(i,j,q)$  from the graph.
3.  $\text{presence\_node} = n(i,k)$   $k$ th molecule is present on the node  $i$ .
4.  $\text{active\_node} = a(i,k)$   $k$ th molecule is active on the node  $i$ .
5.  $\text{presence\_edge} = e(i,j,q,k)$  There is an  $q$ th edge between node  $i$  and  $j$  with  $k$ th molecule present.
6.  $\text{active\_edge} = b(i,j,q,k)$  There is an  $q$ th edge between node  $i$  and  $j$  with  $k$ th molecule active.
7.  $\text{reachability} = r(i,j,k,z)$  Node  $i$  and  $j$  are reachable with  $k$ th molecule present in  $z$  steps.
8.  $\text{pairing\_matrix} = p(k,k')$  Molecule  $k$  and  $k'$  are pairing molecules in the matrix.
9. Type of the Boolean function = sorts (takes  $k-1$  arguments Bool and return Bool)
10. Boolean function on nodes Function ( $\text{fn\_m}, * \text{sorts}$ )
11. Boolean function on edge Function( $\text{fe\_m}, * \text{sorts}$ )

## 2 Regulation on nodes and edges

Regulation of a model is based on the kind of the model under consideration. for example model 1 (-V 1) has two different arbitrary Boolean function dictating the activity of the molecules on edge and nodes and for variation 3 (-V 3) activity on edge is driven by SNARE-SNARE inhibition.

We have build constraints A0, A1 for these two regulations.

A0: No regulation on nodes.

$$\bigwedge_{i,k} n_{i,k} == a_{i,k}$$

A1: No regulation on edges.

$$\bigwedge_{i,j,q,k} e_{i,j,q,k} == b_{i,j,q,k}$$

A0: Boolean regulation on nodes. Activity of a molecule  $k$  on a node is defined as a Boolean function of presence of other molecule present on that node.

$$\bigwedge_{i,k} n_{i,k} \supset a_{i,k} == f_n[k](\bigvee_{k' \neq k} n_{i,k'})$$

A1: Boolean regulation on edges. Activity of a molecule  $k$  on a node is defined as a Boolean function of presence of other molecule present on that node.

$$\bigwedge_{i,j,q,k} e_{i,j,q,k} \supset b_{i,j,q,k} == f_e[k](\bigvee_{k' \neq k} e_{i,j,q,k'})$$

A1: SNARE-SNARE inhibition. Inhibition of the edges are driven by the pairing matrix.

$$\bigwedge_{i,j,q,k} (e_{i,j,q,k} \wedge [(\bigvee_{k'} p_{k,k'} \wedge \bigwedge_{k' \neq k} p_{k,k'} \supset e_{i,j,q,k'})) \supset \neg b_{i,j,q,k})$$

$$\bigwedge_{i,j,q,k} (e_{i,j,q,k} \wedge \neg[(\bigvee_{k'} p_{k,k'} \wedge \bigwedge_{k' \neq k} p_{k,k'} \supset e_{i,j,q,k'})) \supset b_{i,j,q,k})$$

### 3 Basic constraints on the edges and nodes

The edge labels are subset of the node label of source and target compartment.

C0: The edge labels are subset of the node label of source compartment.

$$\bigwedge_{i,j,k} e_{i,j,k} \supset a_{i,k}$$

C1: The edge labels are subset of the node label of target compartment.

$$\bigwedge_{i,q} e_{i,j,k} \supset a_{j,k}$$

C2: Self edges are not allowed.

$$\bigwedge_{i,q} \neg e_{i,i,q}$$

C4: Condition on p\_kk'. Diagonal blocks should be all 0's.

$$\bigwedge_{(x < M/2 \wedge y < M/2) \vee (x > M/2 \wedge y > M/2)} \neg p(x, y)$$

C5: Activity on the node. A molecule should be present to be active on a node.

$$\bigwedge_{i,k} a_{i,k} \supset n_{j,k}$$

### 4 Main constraints

Main constraints to be followed.

F0: An edge has to have one present molecule. F0 looks redundant.

$$\bigwedge_{i,j,q} \bigvee_k e_{i,j,q,k} \supset e_{i,j,q}$$

F1: If molecule is active on an edge then it should be present on the edge.

$$\bigwedge_{i,j,q,k} b_{i,j,q,k} \supset e_{i,j,q,k}$$

### 5 Steady state specification

Each molecule leaving the node on a vesicle should come back to its source node in a cycle, i.e., **for every molecule leaving the node there exists a cycle with that molecule present on *each of the edges and nodes* of the path taken.**

### 5.1 Reachability definition and stability condition

If molecule is active on an edge then it should be present on the edge.

F3: stability condition. Source node is reachable by target node with that molecule present in p steps.

$$\bigwedge_{i,j,k} (\bigvee_q e_{i,j,q,k}) \supset (r_{j,i,k,0} \vee r_{j,i,k,1} \vee \dots \vee r_{j,i,k,p})$$

F2: Reachability definition.

$$\bigwedge_{i,j,k,p} r_{i,j,k,p} \supset (\bigvee_q e_{i,j,q,k} \vee \bigvee_{i \neq i'} (\bigvee_q e_{i,i',q,k}) \wedge r_{i',j,k,p-1})$$

## 6 Fusion rule Formula

Fusion rules consist of two different mechanisms.

1. A **SNARE pairing mechanism** which determines compatible Q-R pairs on vesicles and compartments that can cause fusion.
2. **Regulatory mechanisms** on edges and on nodes (possibly distinct) which regulate SNARE activity based on the presence/absence of other molecules on the corresponding node or edge.

F4: For an edge to be valid, at least one SNARE pair on the vesicle and target compartment must be active, and have a non-zero entry in the pairing matrix.

$$\bigwedge_{i,j,q} e_{i,j,q} \supset \bigvee_{k,k'} (b_{i,j,q,k} \wedge a_{j,k'} \wedge p_{k,k'})$$

F5: To ensure that fusion respects the graph structure by the edge under consideration, it should not be possible to fuse with any other node.

$$\bigwedge_{i,j,k} b_{i,j,k} \supset \neg \bigvee_{j \neq j',k''} (a_{j',k''} \wedge p_{k,k''})$$

## 7 Connectivity

To check the whether that n connected is necessary condition, we remove (drop) n edges from the graph and if it disconnects the graph and we get an assignment we have a n connected satisfying graph. We can go down or up using -C - option.

D0: Only present edges can be dropped.

$$\bigwedge_{i,j,q} d_{i,j,q} \supset e_{i,j,q}$$

D1,D2: We are dropping c edges from the graph. exactly c are dropped.

$$\sum_{i,j,q} d_{i,j,q} == c$$

D3: Graph becomes disconnected. Ensure that there is no path between some nodes i,j in the underlying undirected graph. Different reachability.

$$\bigwedge_{i,j} \neg(r'_{i,j} \vee r'_{j,i})$$

D4: New reachability definition for grph connectedness: dReachable. Node i,j are reachable either if there is a direct edge and its not dropped. Or there is an node i' such that, there is a direct edge between i,i' which is not dropped and i' and j is dReachable.

$$\bigwedge_{i,j} [\bigvee_q (e_{i,j,q} \wedge \neg d_{i,j,q}) \vee (\bigvee_{i' \neq i} r'(i',j) \wedge \bigvee_q (e_{i,i',q} \wedge \neg d_{i,i',q}))] \supset r'(i,j)$$