

Hands-on session

SBGN maps with SBGN-ED

The SBGN workshop, 24th September 2016, Newcastle upon Tyne

Intro

The Systems Biology Graphical Notation, SBGN, is a standard format to represent biological networks visually. SBGN diagrams contain agreed-upon glyphs. Once you know these glyphs, it is easy to read and exchange meaningful diagrams encoding biological information.

The SBGN workshop aims to introduce scientists to the SBGN. The first part features introductory talks to the SBGN family of standards, and to software tools that offer SBGN support. The second part is dedicated to hands-on sessions that allow you to try out SBGN software.

Today, you will learn how to create SBGN-compliant diagrams.

We will also have a competition for the best SBGN map!

During the following exercises:

1. please save your maps as GML and GraphML format to not lose any information,
2. you can have several maps opened in VANTED. You can tile or cascade them (*Window* → *Tile / Cascade*),
3. if any problem, let us know.

I DOWNLOAD AND INSTALLATION OF SBGN-ED (10-15min)

For those of you who already have VANTED and SBGN-ED installed, you can directly go to Section II.

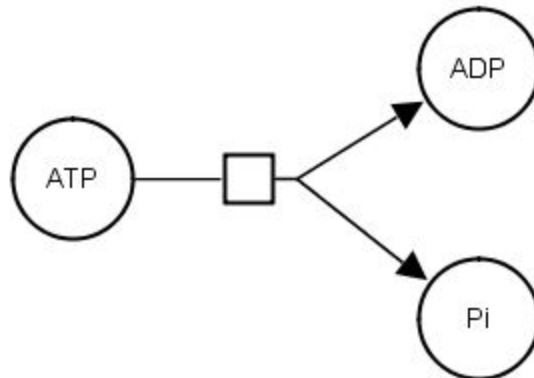
1. Download and install VANTED 2.6.3 on your system:
<https://immersive-analytics.infotech.monash.edu/vanted/index.php?file=doc2.html>
2. Download SBGN-ED 1.6 (sbgn-ed.jar):
<https://immersive-analytics.infotech.monash.edu/vanted/addons/sbgn-ed/downloads/sbgn-ed.jar>
3. Launch VANTED.

4. Install SBGN-ED:
 - a. Go to *Edit* → *Preferences*.
 - b. On the left panel, go to *Addon Manager*.
 - c. Click *Install / Configure Add-ons*.
 - d. Click *Install Add-on*.
 - e. Choose the **sbgn-ed.jar** downloaded previously.
 - f. Click *Install*, then *OK*, and *Ok*.

Congratulations! You are now able to use SBGN-ED to generate SBGN maps.

II DRAWING A SMALL NETWORK (10min)

To begin with VANTED and SBGN-ED, draw the following simple network (shown in the SBGN-ED presentation).



Reminder: VANTED has two modes: *Create nodes and edges* and, *Select nodes and edges* (see Fig. 1 below). To be able to select your nodes, you must first change the mode in VANTED to *Select nodes and edges*.

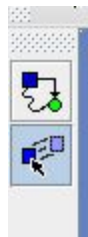


Fig. 1 Mode buttons in VANTED. The top button creates node and edges. The bottom button (selected in the figure) selects nodes and edges.

III TRANSLATION OF A MODEL FROM BIOMODELS INTO SBGN + LAYOUTING (30min)

BioModels: <https://www.ebi.ac.uk/biomodels-main/>

SBML: http://sbml.org/Main_Page

Biomodels gathers computational models of biological processes. The models are manually curated and enriched with annotations. They are available in the standard model encoding format SBML (Systems Biology Markup Language). SBML stores information about the biological processes in a XML-based format, with the aim of simulating the models.

You can use VANTED to import and visualise any model from Biomodels:

1. Import the model
 - a. Go to tab *Pathways – Biomodels*.
 - b. In the dropdown list, select *Biomodels Id*.
 - c. Search for: **BIOMD0000000012**.
 - d. Double click on the desired model to load it.

Hint: You may also get the model(s) directly from the Biomodels website at: <http://biomodels.caltech.edu/>

Note: The reaction network underlying the model is now visualised. However, the visualisation is done using the generic layout tools provided by VANTED. It is *not yet* SBGN-compliant.

2. Translation SBML → SBGN
 - a. Go to tab *SBGN-ED - Tools*
 - b. In section Translation, click on *Translate SBML to SBGN*

Question: How did your model change after conversion from SBML to SBGN?

Questions: Any problems that you observed?

In SBML, models are usually automatically generated and do not have a layout provided. This is why your SBGN-compliant network is not yet nicely represented. To counteract this, you can either manually rearrange your network or try to apply an automatic layout:

3. Apply an automatic layout
 - a. Go to tab *Layout*
 - b. Select *Force Directed*
 - c. Click on *Layout Network*

Note: Currently, there are no layout that automatically generates a comprehensive design of biological maps as a human would do manually. This is a major task that needs to be resolved. Manual layout is often very efficient, but time-consuming for large networks.

Hint: You can try the different layouts available and see which one satisfies you most. Otherwise, a manual layout is feasible in this case.

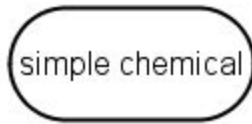
Don't forget to save your model as .gml or .graphml, and as .sbgn . File → Save as → (Careful on the type Files of Type) → Save as...

IV IMPORTANCE OF SBO TERMS (30min)

SBO browser online: <http://bioportal.bioontology.org/ontologies/SBO>

SBO terms form a controlled vocabulary that can be used to semantically annotate model elements to biological and mathematical concepts. SBO terms are used in SBGN to state the type of a biological entity or the type of a reaction. They are added to glyphs and arcs.

For example, a simple chemical in SBGN PD is characterised by the SBO term: SBO:0000247.



We have provided the BIOMD0000000012 example without the SBO terms BIOMD0000000012-noSBO.xml. Re-do the steps from **III - 2.** to **III - 3.**

Note: VANTED enables you to apply a layout from a layouted file.

Instead of re-doing manually your previous layout (III-3.), you could:

1. Go to tab *Layout*
2. Select *Apply From Layouted File*
3. Click on *Layout Network*, then *OK*
4. Select the layouted model you saved in **III** and click on *Open*

Compare the two maps you have generated so far.

What are the main differences that you can see?

Again, don't forget to keep track of your network, save it.

V COLORS IN SBGN (20min)

It is possible to color your map to improve readability. There are no rules defined. It is up to you to associate colors to glyphs and arcs.

1. Open your model from II (if not already the case).
2. Select the node or edge you would like to color
(for multiple selection: Ctrl + mouse left click).
3. Go to tab *Attributes*
Select sub-tab *Node* or *Edge* (depending on what type you have selected).
4. Color the selected element as you wish.

Once you are satisfied with your network,

1. Save your map as (*File* → *Save as*):
 - a. SBGN-ML
 - b. GML
 - c. GraphML
2. Close your network
3. Open the SBGN-ML, GML and GraphML file (*File* → *Open*).

What differences can you spot? What can you conclude?

VI IMAGE EXPORT (15min)

VANTED allows you to export your maps into different image type: PNG, PDF, SVG, JPG.

For that purpose, follow the next steps:

1. Go to *File* – *Export* – *Network as image*.
2. Select the type you want.
3. Fix the parameters and play around with them to see the difference.

VII CREATE A MAP FROM THE LITERATURE – COMPETITION MAP (1h00-1h30)

Models described in scientific papers often do not contain a visual representation summarising the network or if it does, most of the time you will have a representation not standardised. In this exercise, you will recreate an SBGN map from an article:

A. Goldbeter. A model for circadian oscillations in the Drosophila period protein (PER). Proceedings of the Royal Society of London B: Biological Sciences, 261(1362):319–324, 1995.

Suggestion of steps to follow:

1. Read carefully and try to find *keywords* related to the model. Ask yourself:
 - a. What are the entities involved?
 - b. How do they interact?

2. Sketch how you want to visualise the model, the entities and the relationships.
Hint: Do not forget to consider the compartments.

3. Start building brick by brick the model in SBGN-ED: create nodes involved in a reaction then the relationships among them.
4. Link the bricks if not already the case.
5. Layout your network, add colors if you wish.
6. Export your model and send it to: vasundra.toure@uni-rostock.de, so that it can enter the competition.