# Modelling with Petri Nets: Case Studies
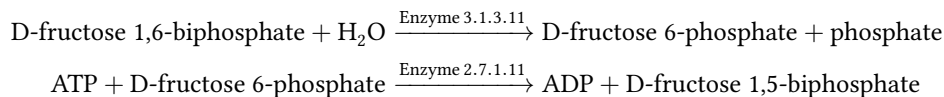
## Network Medicine

http://lacl.fr/~sivanov/doku.php?id=en:pn-biomodelling

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## Case 1: Glycolysis Pathway

Glycolysis is the metabolic pathway that converts glucose $C_6H_{12}O_6$ into pyruvate $CH_3COCOO^-$ + $H^+$ [3]. The free energy released in this process is used to form the high-energy molecules ATP and NADH. According to the KEGG database [4], this pathway includes the following two reactions:

$$\text{D-fructose 1,6-biphosphate} + H_2O \xrightarrow{\text{Enzyme 3.1.3.11}} \text{D-fructose 6-phosphate} + \text{phosphate}$$

$$\text{ATP} + \text{D-fructose 6-phosphate} \xrightarrow{\text{Enzyme 2.7.1.11}} \text{ADP} + \text{D-fructose 1,5-biphosphate}$$

1. Represent the interactions induced by these equations in a Petri net.

2. Draw the Petri net using one of the suggested software tools (see below) and explore its dynamic behaviour under the asynchronous mode.

3. Check some dynamic properties of the resulting Petri net.

For more details on this example, see [1, Section 4.1.1].

## Case 2: Kinase (MAPK) Cascade

The mitogen-activated protein kinase cascade is the core of the ubiquitous ERK/MAPK pathway that can transmit various signals (cell division, differentiation, etc. [2, Section 3]) from the cell membrane to the nucleus. Figure 1 (next page) describes the typical modular structure of this pathway. In each layer, forward reactions are catalysed by kinases and reverse reactions by phosphatases. RasGTP is considered to be the input signal and ERKPP the output signal.

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## Software Tools

The tool software tool I had in mind when designing this assignment is *Tina*: Time Petri Net Analyser. It can be downloaded here:

http://projects.laas.fr/tina//download.php

Once you have downloaded the archive, unpack it, go under the directory `bin` and launch the file called `nd`. You should be presented with a window having a workspace, a toolbar, and a menu
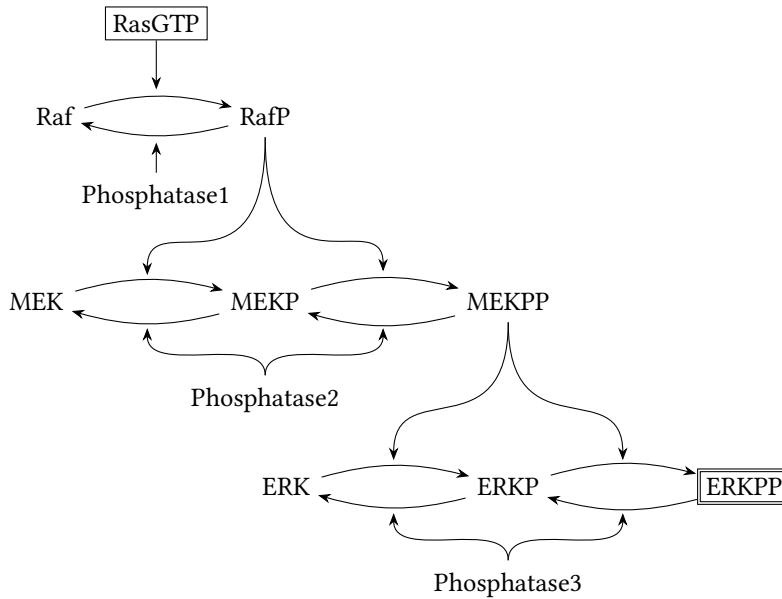
Figure 1: The general scheme of the MAPK cascade. Redrawn from [2, Fig. 3].

bar. To create a place, click on the button with a circle on it. To create a transition, click on the button with a square on it. To add an arc, click on the button with a black horizontal arrow, then click on a place and drag the mouse to the transition you want to connect it to. To add tokens to a place, right-click on it and, in the popup window, modify the number in the field "marking".

To run the Petri net, go to the "Tools" menu and choose "stepper simulator". This will show you a window in which the enabled transitions will be highlighted in red. Click on one of the enabled transitions to run it once.

If you are feeling curious (and lucky), you may also check out the rather long list of different Petri net-related software tools:

`https://www.informatik.uni-hamburg.de/TGI/PetriNets/tools/quick.html`

# References

[1] Paolo Baldan, Nicoletta Cocco, Andrea Marin, and Marta Simeoni. Petri nets for modelling metabolic pathways: a survey. *Natural Computing*, 9(4):955–989, Dec 2010. Draft available at `http://www.math.unipd.it/~baldan/Papers/Soft-copy-pdf/BioPN.pdf`.

[2] Monika Heiner, David Gilbert, and Robin Donaldson. Petri nets for systems and synthetic biology. In Marco Bernardo, Pierpaolo Degano, and Gianluigi Zavattaro, editors, *Formal Methods for Computational Systems Biology: 8th International School on Formal Methods for the Design of Computer, Communication, and Software Systems, SFM 2008 Bertinoro, Italy, June 2-7, 2008 Advanced Lectures*, pages 215–264. Springer Berlin Heidelberg, Berlin, Heidelberg, 2008. Available on Research Gate.

[3] Wikipedia. Glycolysis — Wikipedia, The Free Encyclopedia, 2017. [Online; accessed 4-November-2017].

[4] The KEGG pathway database. `http://www.genome.jp/kegg/pathway.html`.