Project 3: Triggering and Blocking apoptosis

Background

Apoptosis, often referred to as programmed cell death, is a highly regulated cellular process crucial for maintaining tissue homeostasis, development, and immune response. It serves as a mechanism to eliminate damaged, infected, or unnecessary cells without triggering inflammation or damage to neighboring cells. Apoptosis is characterized by a series of orchestrated events, including condensation of the cell and its nucleus, fragmentation of DNA, and formation of apoptotic bodies which are subsequently engulfed and cleared by phagocytes. This process is tightly controlled by a variety of signaling pathways involving both pro-apoptotic and anti-apoptotic molecules, ensuring the proper balance between cell survival and death. Dysregulation of apoptosis can contribute to various pathological conditions, including cancer, autoimmune diseases, and neurodegenerative disorders, highlighting its importance in maintaining cellular and organismal health. Finding intervention targets, either to force the activation of apoptosis or to prevent it, are thus important objectives.

Suggested aims

• Import the Apoptosis map from:
https://github.com/colomoto/colomoto-docker/raw/master/tutorials/CaSQ/Apoptosis_VS_SSA_AN.xml
• Open it in CellDesigner and list the input nodes and phenotype nodes
• Convert it to SBML-qual using CaSQ
• Import the SBML-qual model into WebMaBoSS or pyMaBoSS
• Simulate the model with random conditions. What percentage of conditions activates the Apoptosis phenotype ?
• This phenotype is activated by two possible conditions of inputs: One single input node, and one combination of input nodes. Can you find which ones ?
• Use the sensitivity analysis to test possible mutants, and list which ones inactivates Apoptosis, for each combination of inputs
• You can also repeat these steps using the Panther apoptosis map:
https://www.pantherdb.org/pathway/pathwayDiagram.jsp?catAccession=P00006
• Can you find some mutants which are common to both maps/models ?

Additional Resources

• WebMaBoSS: http://maboss.curie.fr/webmaboss/
• pyMaBoSS: https://pymaboss.readthedocs.io/en/latest/