Sections 5.3.3.1 and 5.3.3.2 to simplify the network to contain 267 nodes and 751 arcs.

Saadatpour *et al.* [18] further investigated the T-LGL network and found that 14 nodes of the network have high importance in the sense that blocking any of these nodes disrupts (almost) all signaling paths from the complementary node to apoptosis, thus providing these nodes as possible candidate therapeutic targets. All of these nodes are also found to be essential for the T-LGL survival state according to a dynamic model, *i.e.*, reversing their states causes apoptosis to be the *only possible* outcome of the system. Moreover, experimental verification of the importance of these nodes exists for 10 of the 14 nodes [18].

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EXERCISES

7.1 The purpose of this exercise is to get the reader familiar with the algorithmic framework shown in Fig. 5.4 and the NET-SYNTHESIS software in [14] that uses this algorithmic framework. Consider the following small subset of the interactions reported in [15]:

$$\begin{aligned}
&\text{ABA} \dashv \text{NO}\\
&\text{ABA} \rightarrow \text{PLD}\\
&\text{ABA} \rightarrow \text{GPA1}\\
&\text{ABA} \rightarrow \text{PLC}\\
&\text{GPA1} \rightarrow \text{PLD}\\
&\text{PLD} \rightarrow \text{PA}\\
&\text{NO} \dashv \text{KOUT}\\
&\text{KOUT} \rightarrow \text{Closure}\\
&\text{PA} \rightarrow \text{Closure}\\
&\text{PLC} \rightarrow (\text{ABA} \rightarrow \text{KOUT})
\end{aligned}$$

For each of the following tasks, report the network generated and verify that it is correct.

a) Generate the network using only the direct interactions and perform transitive reduction on the graph (*e.g.*, in NET-SYNTHESIS software, select "Reduction (slower)" from the Action menu).

b) Add double-causal inferences to the network (*e.g.*, in NET-SYNTHESIS software, select "Add pseudonodes" from the Action menu).