IGF is considered as an input of the network.
IGF binds to its tyrosine kinase receptor on the cell membrane, the receptor sequesters IRS (insulin receptor substrate – via Grb and SOS, which are not included in the model). There is a negative feedback loop from S6K to IRS.
IRS interacts with a regulatory domain of PI3K (Phosphoinositide 3 Kinase) and activates it. Rho forms an inhibitory feedback loop on PI3K (through ROCK and PTEN, which are not included in the model).
Akt is activated by PI3K. mTORC2 can also activate Akt independently (to enable intracellular glucose metabolism).
Akt phosphorylates and inhibits TSC2 (Tuberous Sclerosis Factor 2), as does mTORC2.
TSC2 inhibits mTORC1 (mammalian Target of Rapamycin complex 1). Rac is needed for mTORC1 activation.
S6K is one of the substrates of (activated by) mTORC1.
Phosphorylation by PI3K as well as contact with Rac and TSC2 are needed for mTORC2 activation. It is unknown if all or just some factors are needed for activation. We therefore assume that the majority of these factors must be present. S6K inhibits mTORC2 through phosphorylation.
PI3K, mTORC2 and TSC2 are able to activate Rac (a small GTPase). Rho and Rac inhibit each other and cannot exist in the same compartment at the same time. We therefore require Rho to be absent in the majority of the last three time steps.
PI3K and mTORC2 are able to activate Rho (a small GTPase). Rho and Rac inhibit each other and cannot exist in the same compartment at the same time. We therefore require Rac to be absent in the majority of the last three time steps.