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Boolean Modeling of Serotonin mediated Ca^{2+} Signaling pathway

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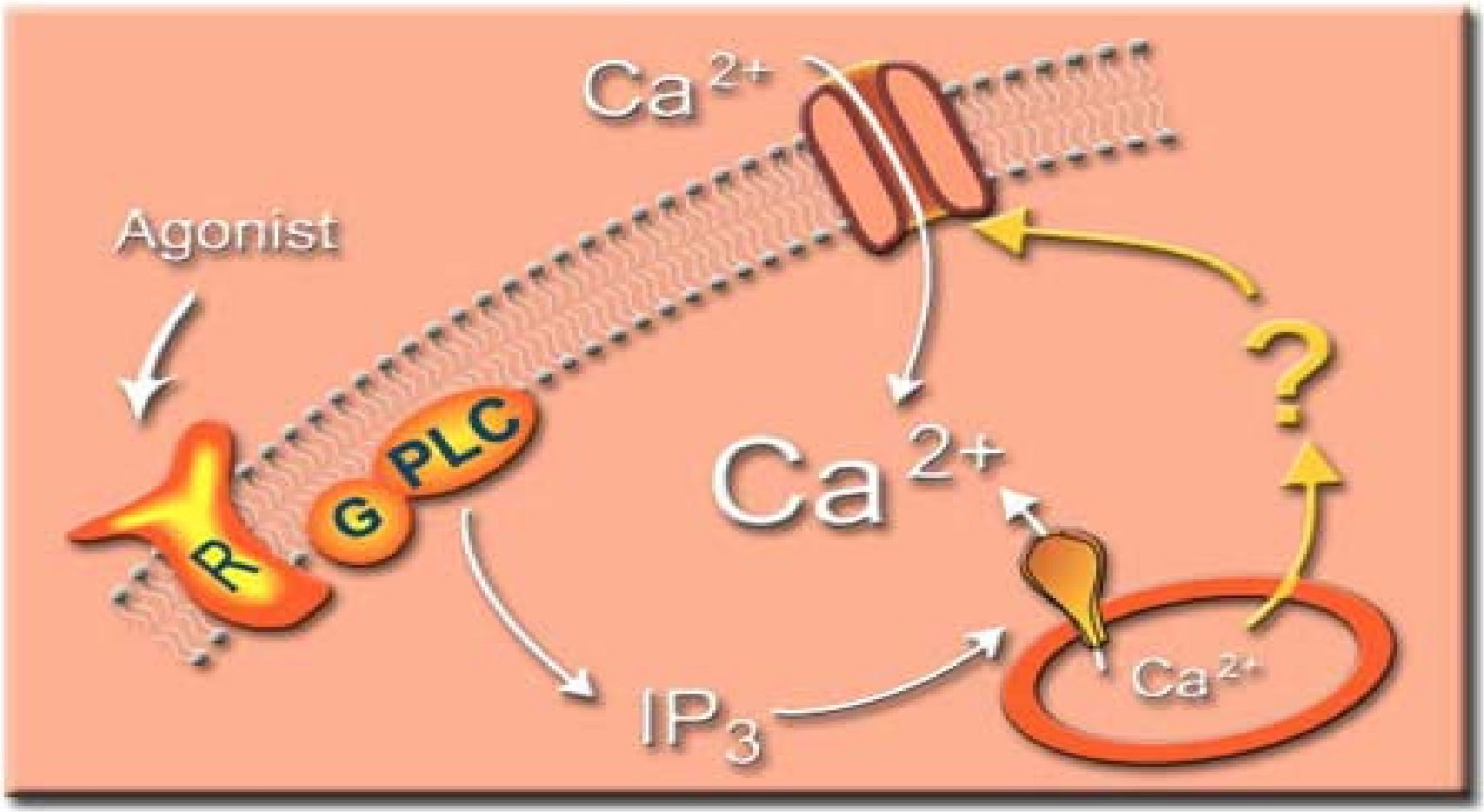
Calcium Signaling



http://dir.niehs.nih.gov/dirlst/images/fig-putney.jpg

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Calcium Signaling in neuroscience

- Ca^{2+} is key secondary messenger in neuronal guidance
- Short term responses such as changes in growth cone guidance, rearrangement of cytoskeleton, neurotransmitter release
- Long term responses: Gene transcription leading to terminal differentiation.

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Altered Calcium Signaling Effects

Normal Physiological

- Neurotransmitter Release
- Long Term Potentiation
- Long Term Differentiation

Pathophysiological

- Epilepsy
- Alzheimer's
- Ataxia

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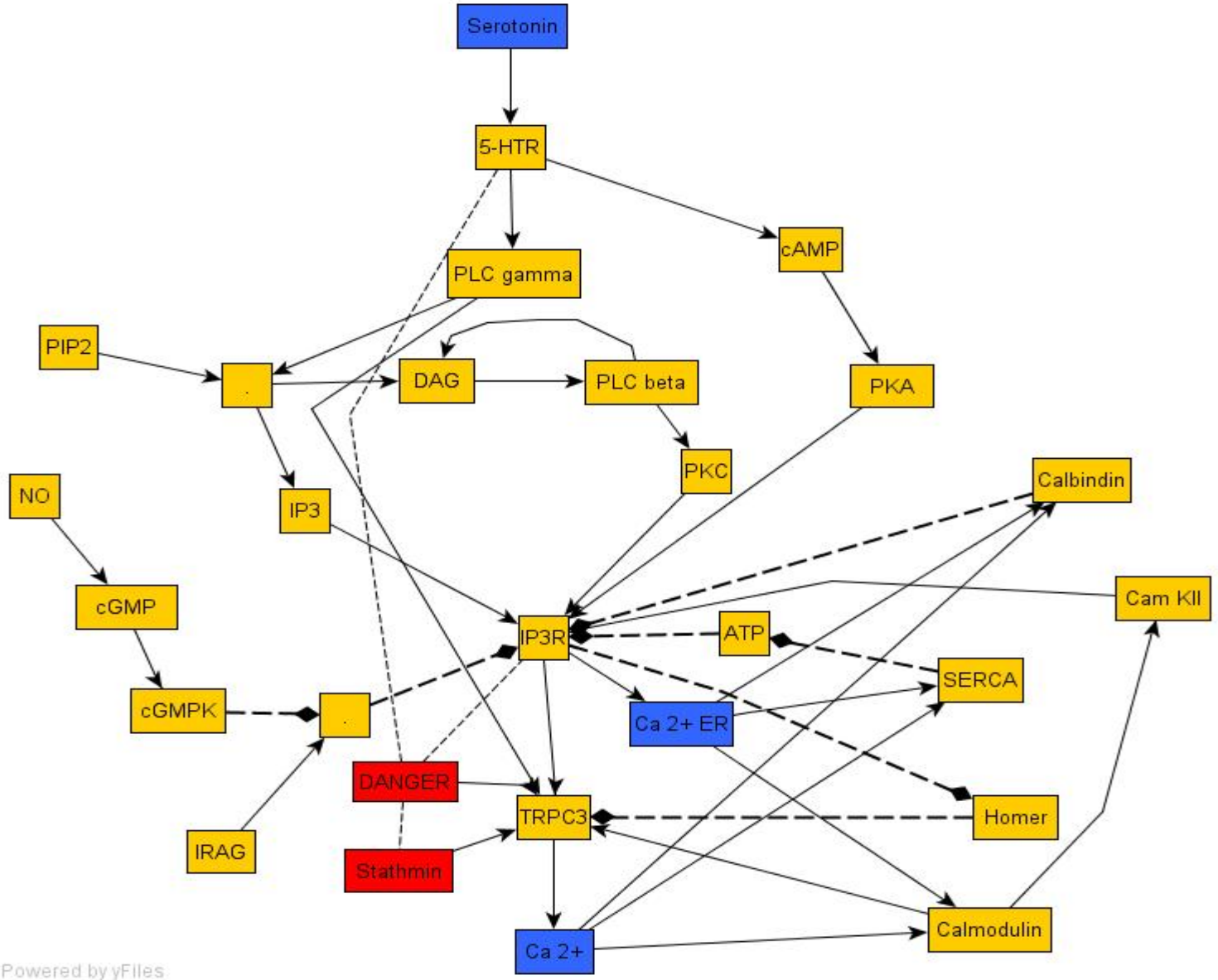
Serotonin

- 5- hydroxytryptamine is important signal for neuronal development.

- Activates a Calcium signaling cascade similar to Nerve growth factor (NGF)

Serotonin mediated calcium signaling network



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Network Characteristics

- 26 nodes, 2 process nodes, 42 edges.
- IP_3R, TRPC3 are most connected nodes.
- Feed Forward and Feedback loops show that the process is highly regulated.

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Rules for Boolean Modeling

- **5-HTR*** = Serotonin
- **PLCγ*** = 5-HTR or DAG
- **cAMP*** = 5-HTR
- **PKA*** = cAMP
- **DAG*** = PIP2 and (PLCβ or PLCγ)
- **PLCβ*** = DAG
- **IP_3*** = PIP_2 and (PLCβ or PLCγ)
- **cGMP*** = NO
- **cGMPK*** = cGMP
- **PKC*** = (PLCβ or PLCγ) and/or (Ca^{2+} or Ca^{2+}ER)
- **TRPC3*** = [(IP_3R and PLCγ and CaM) and not HOMER] and Stathmin
- **HOMER***= not IP_3R
- **Ca^{2+}*** = TRPC3
- **CaM*** = Ca^{2+} or Ca^{2+}ER
- **Ca^{2+}ER*** = IP_3R
- **SERCA*** = Ca^{2+} or Ca^{2+}ER
- **ATP*** = not SERCA
- **Calbindin*** = Ca^{2+} or Ca^{2+}ER
- **CamkII*** = Ca^{2+} or Ca^{2+}ER
- **IP_3R*** = (IP_3 and DANGER) or (IP_3 and DANGER and CamkII) or (IRAG and not cGMPK) or (not ATP) or (not Calbindin)
- **DANGER*** = 5- HTR

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Next?!!

- Boolean Modeling using synchronous and asynchronous update.
- Steps needed to reach steady state. (oscillations in this case)
- Can mutant behavior be modeled. (DANGER KO, etc.)

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