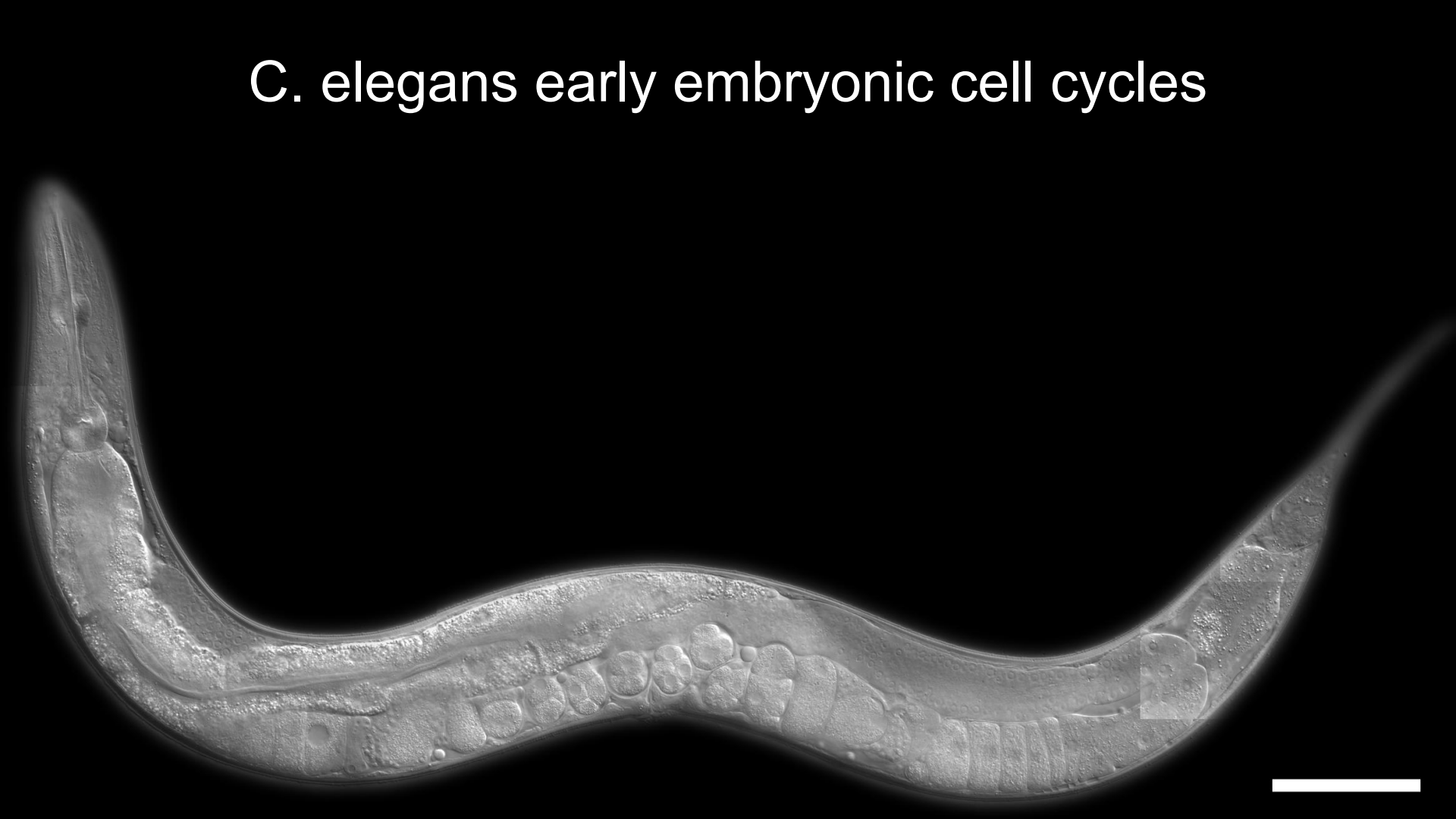
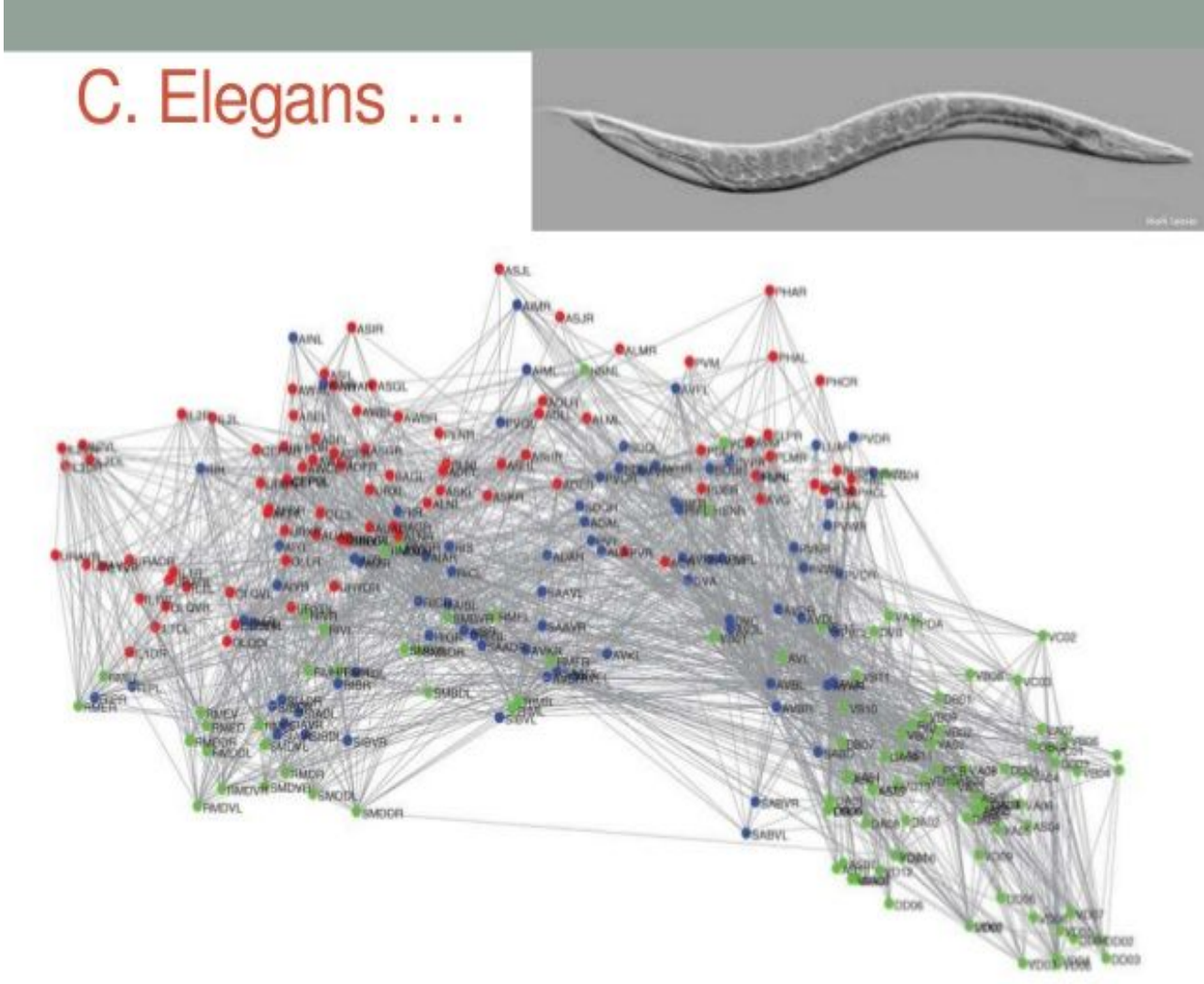
C. elegans early embryonic cell cycles



Background: A Popular Model Organism

- First multicellular organism to have its genome completely sequenced
- Has had its “connectome”, the wiring of its 302 neurons, mapped. The resulting network has small world properties.



What is being modeled in my project?

C. elegans cell cycle, late embryo/ larval stages

Phase 1: Gap 1

Phase 2: Synthesis (genome duplicates)

Phase 3: Gap 2

Phase 4: Mitosis (cell divides into daughter cells)

C. elegans cell cycle, ~~late embryo/ larval stages~~ early embryo development

~~Phase 1: Gap 1~~

Phase 2: Synthesis (genome duplicates)

~~Phase 3: Gap 2~~

Phase 4: Mitosis (cell divides into daughter cells)

What will the nodes represent?

~600 genes related to cell-cycles in C. elegans

“The core regulatory mechanism is related to the activity of complexes of CDKs (cyclin-dependent kinase) and cyclins.”

1. CDKs = enzymes = proteins
2. Cyclins = proteins

“We combine several genes or proteins into one node based on their biological functions.”

3. Inhibitors (e.g. Cki-1)
4. Degraders (e.g. Cul-1, lin-23)

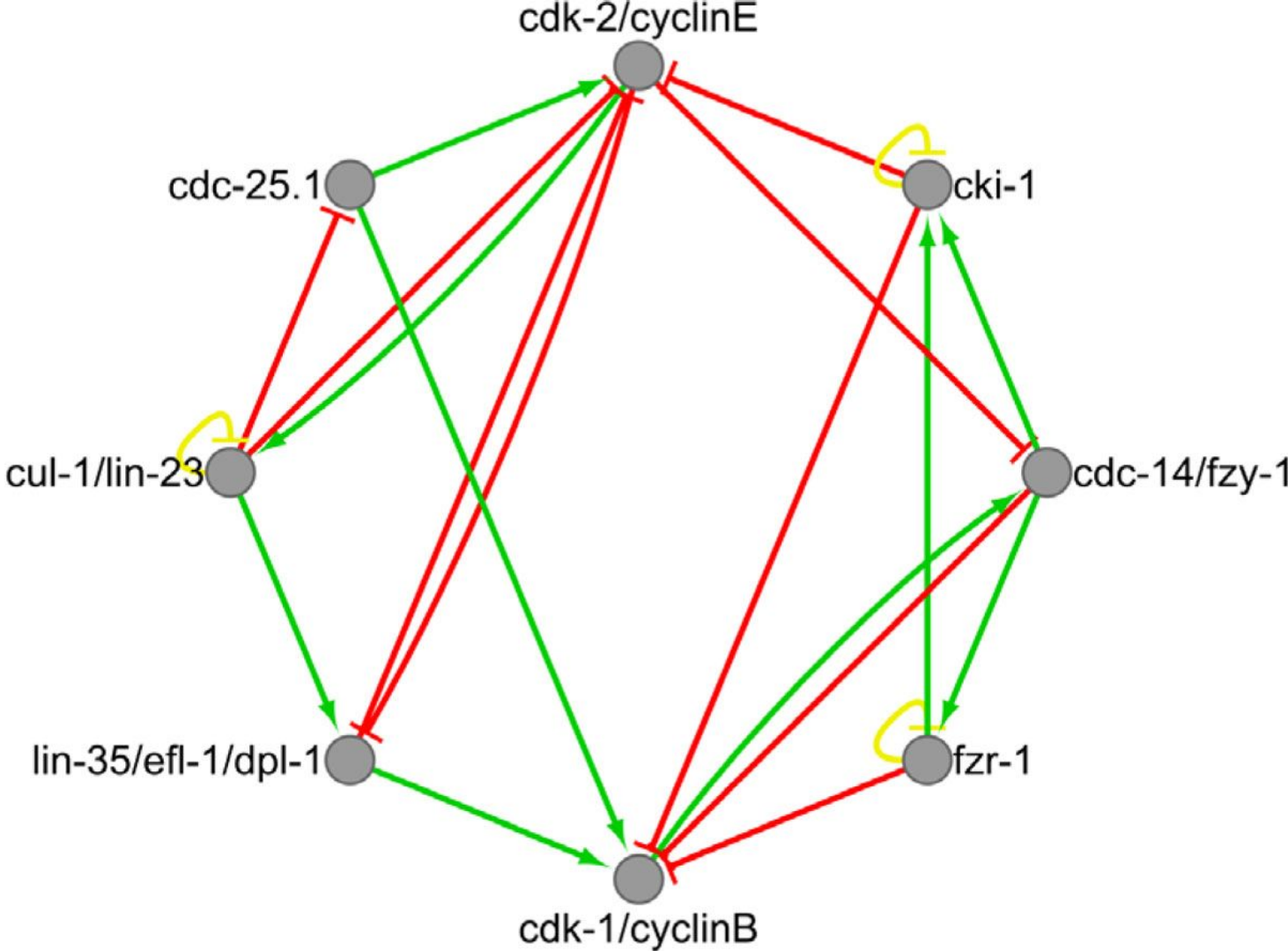
Nodes = 8

Red Edge = Deactivation (-1)

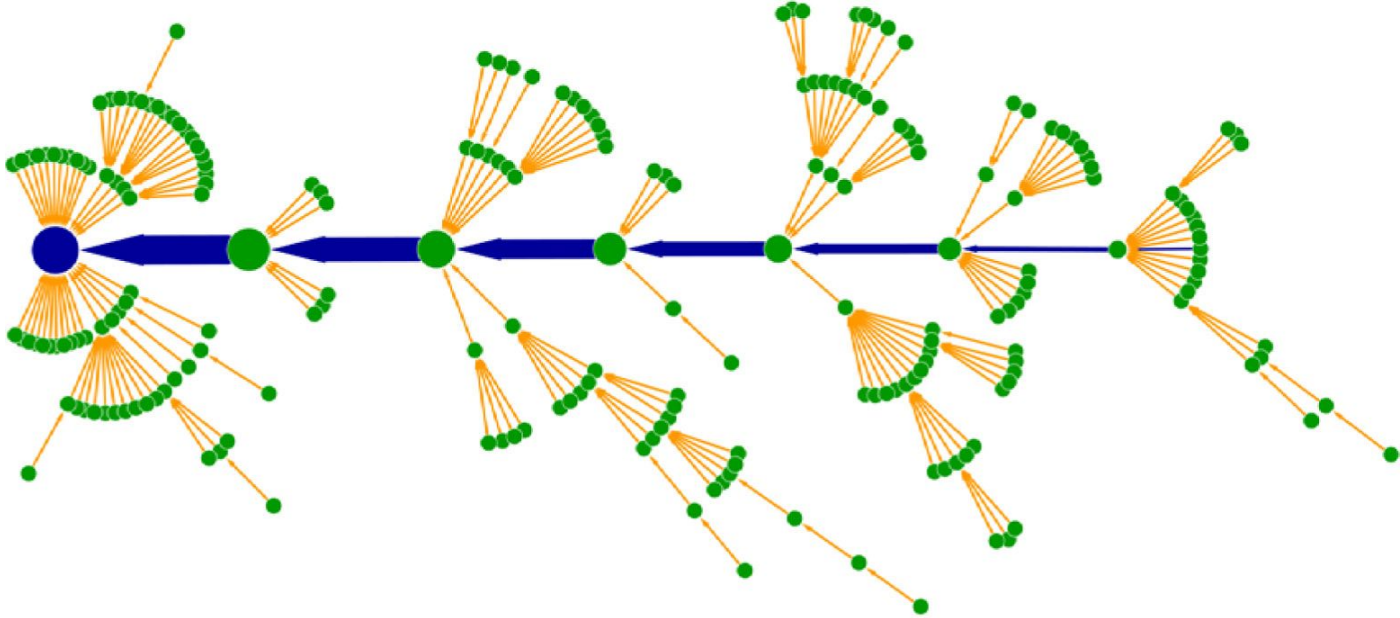
Green Edge = Activation (1)

Yellow Edge = Self Degradation (-1)

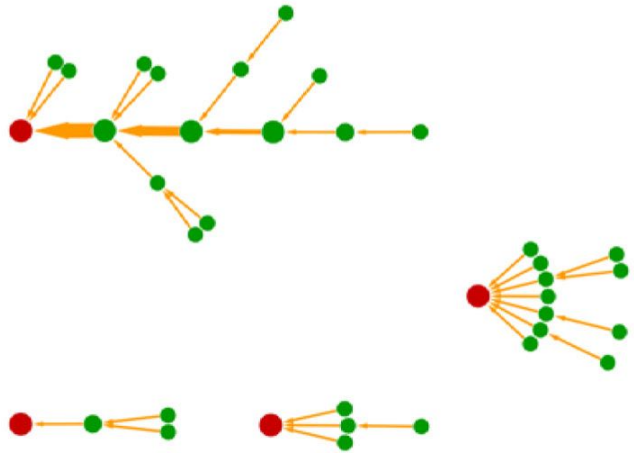
Node Threshold = 0



$2^8 = 256$ possible initial states



Largest Attractor Basin Size = 219 (85.5% of possible states)



Comparison with Random Networks

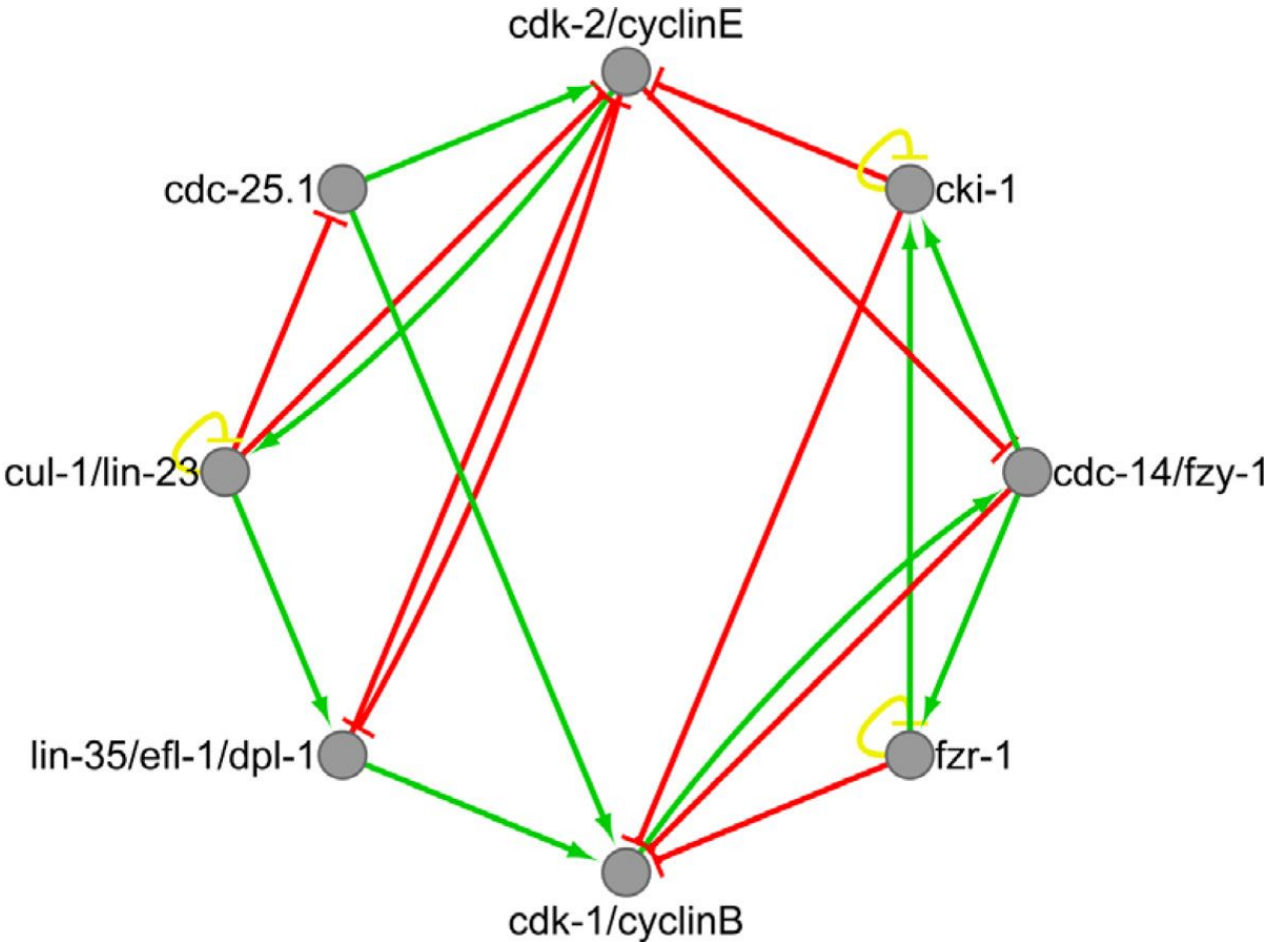
- Researchers generated 1,000 same-sized random networks.
  - Same number of nodes
  - Same number of activation and repression edges

- Average number of attractors in random network = 17.57
  (5 attractors in C. elegans network)
- Average basin size of largest attractor in random network = 105.56
  (Largest basin in C. elegans network contains 219 initial states)
- Of 1,000 random networks, 1.1% contain larger basin size than C. elegans network

Gene Knock Down Experiment

40.3 minutes to complete cell cycle

Wild Type

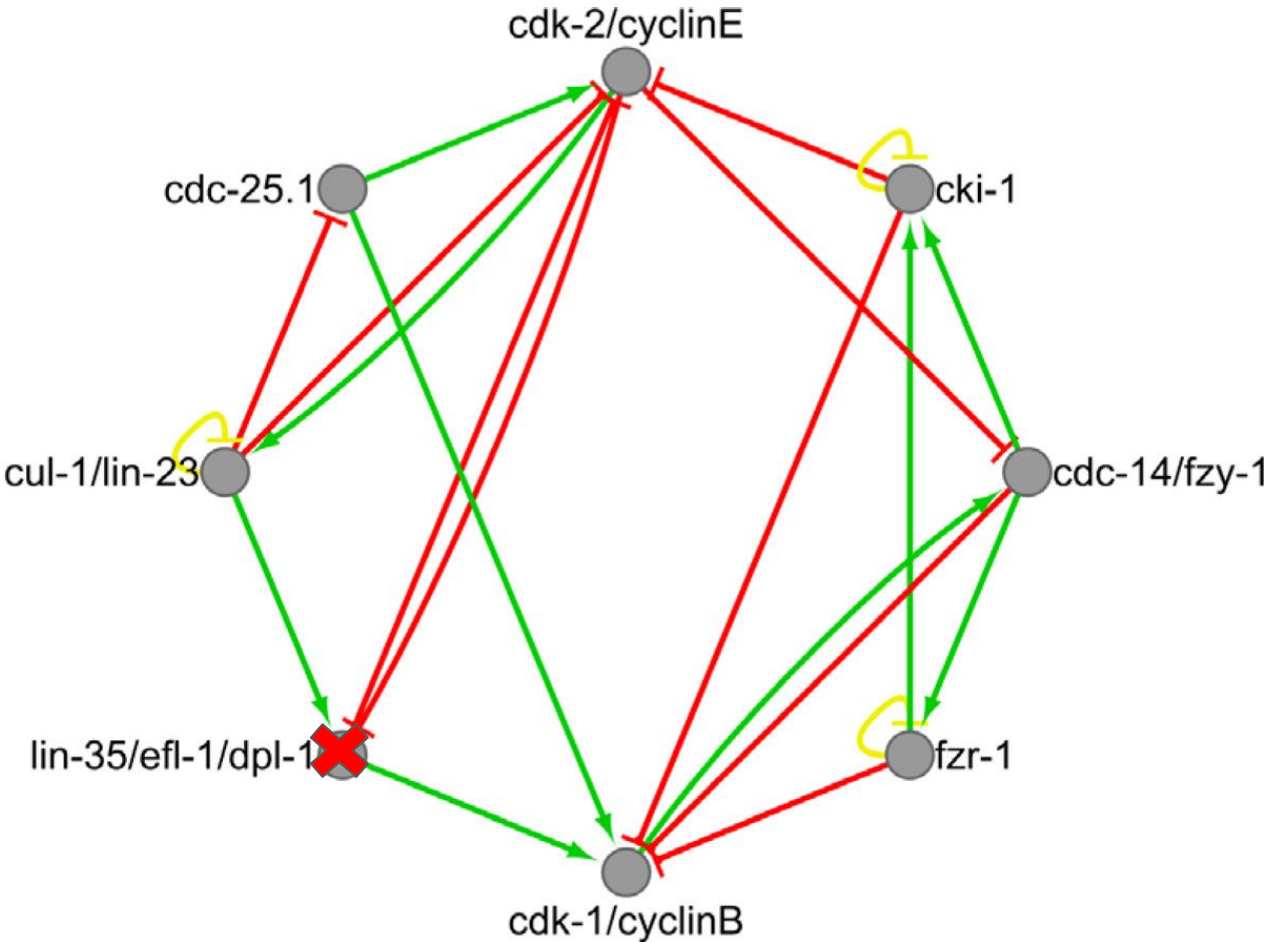


Gene Knock Down Experiment

efl-1 knock down = 27.1 minutes

wild type cycle = 40.3 mintues

Mutant Type

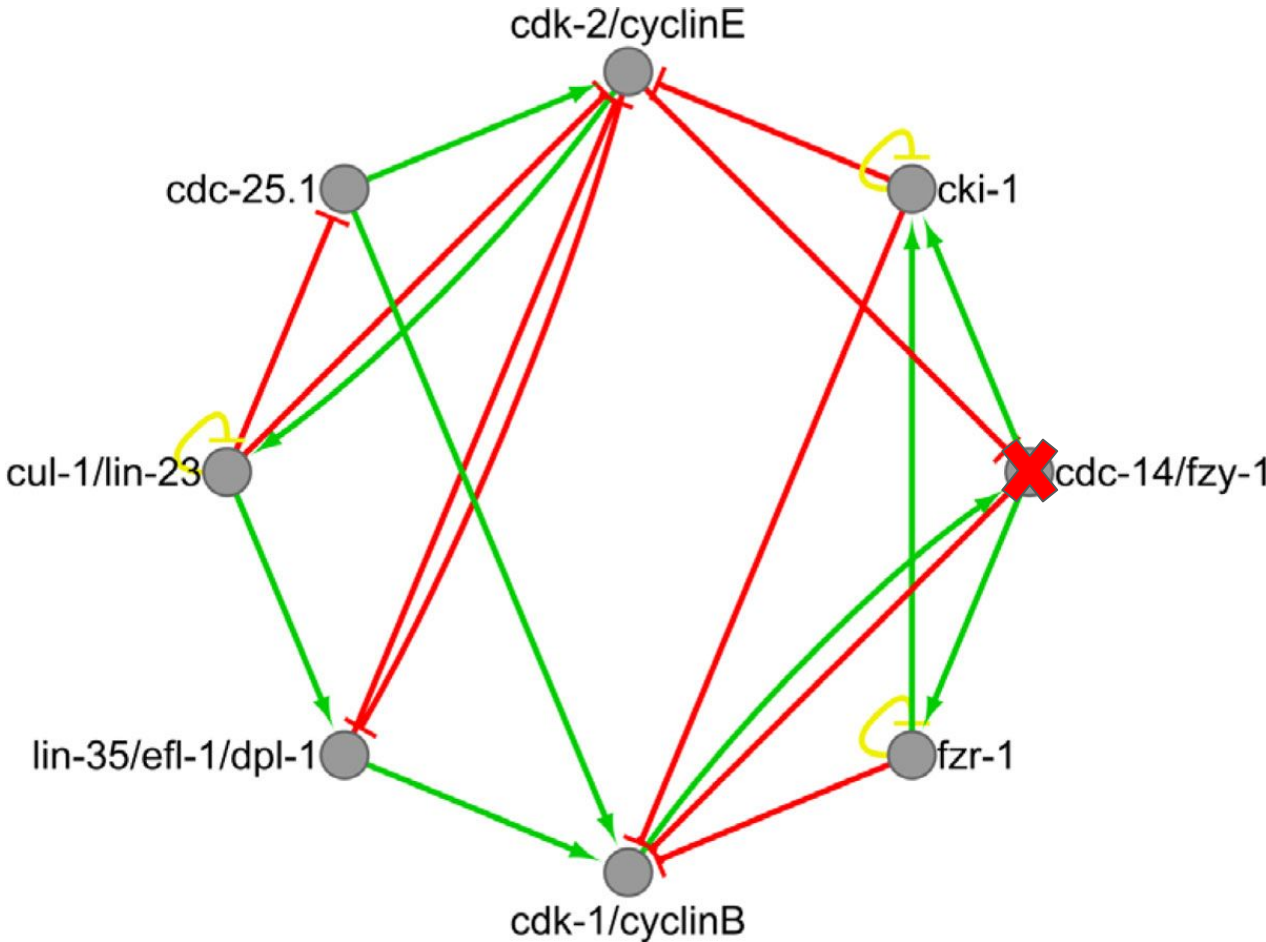


Gene Knock Down Experiment

cdc-14 knock down = 25.4 minutes

wild type cycle = 40.3 mintues

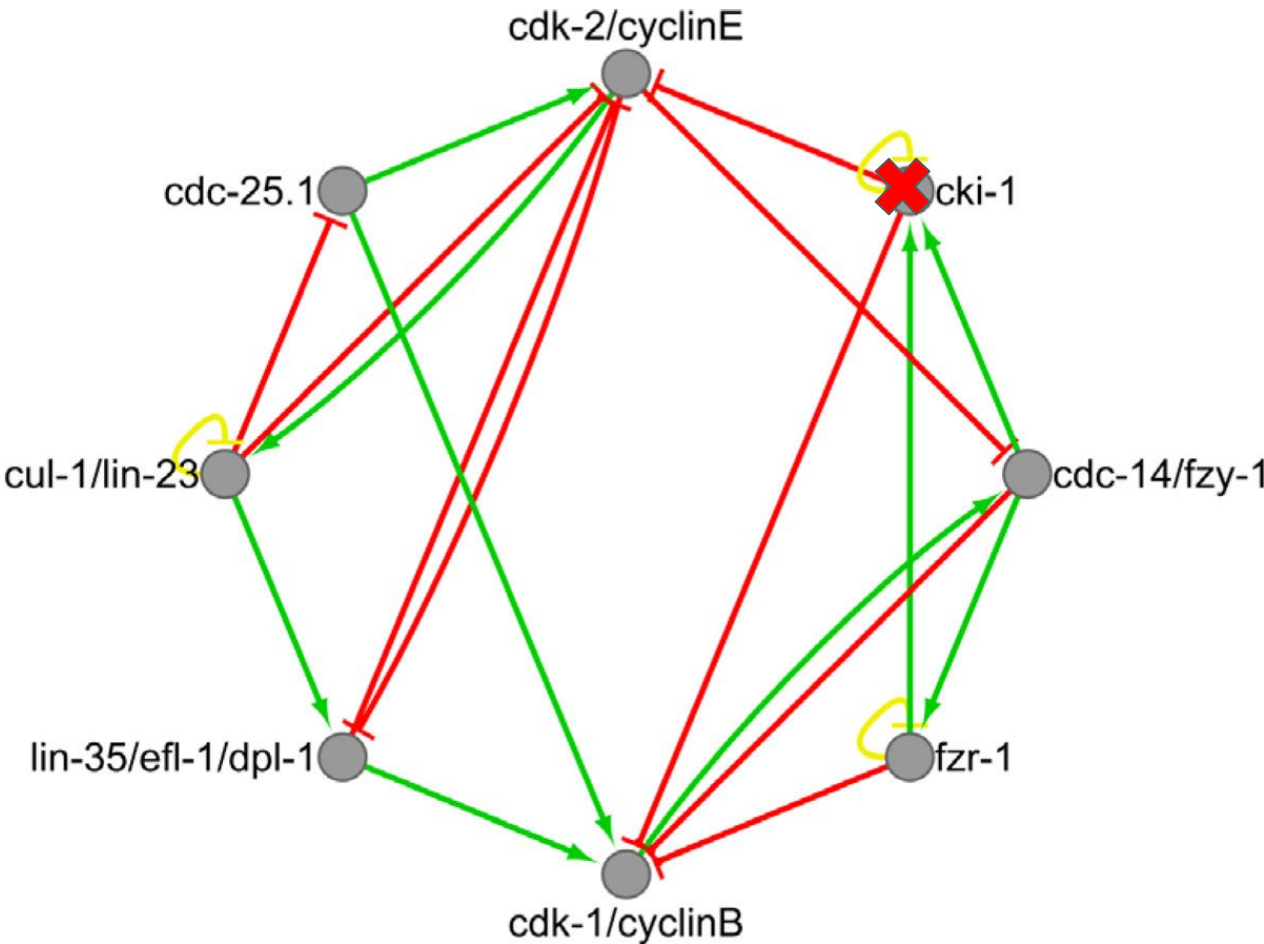
Mutant Type



Gene Knock Down Experiment

cki-1 knock down = 27.7 minutes

wild type cycle = 40.3 mintues



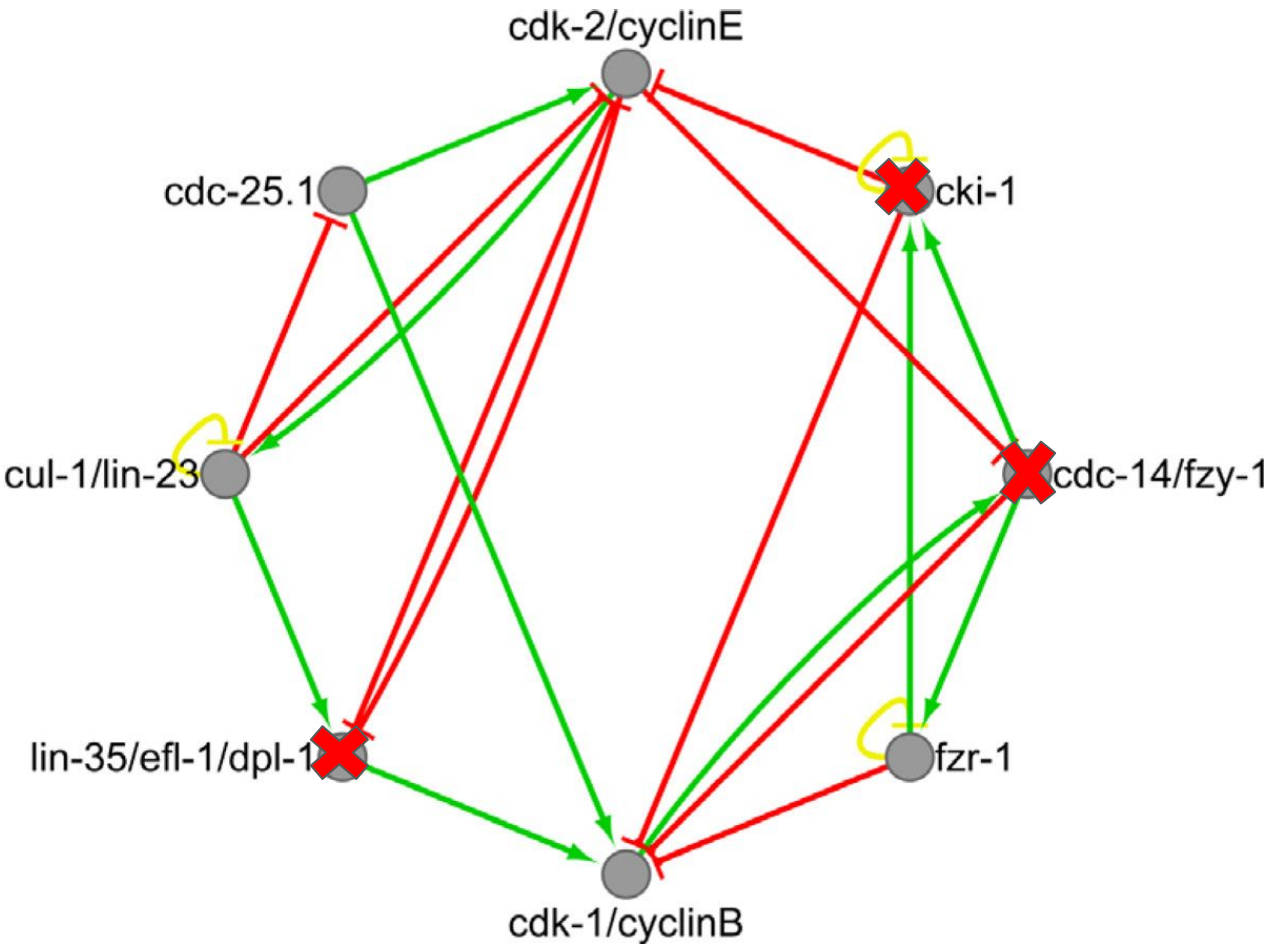
Gene Knock Down Experiment

efl-1 knock down = 27.1 minutes

cdc-14 knock down = 25.4 minutes

cki-1 knock down = 27.7 minutes

wild type cycle = 40.3 mintues



Gene Knock Down Experiment: Network Results

- Researchers modeled gene knock down experiment by forcing the node representing a “knocked down” gene to 0 at each time step.
- When node cdc-14 was knocked down the number of attractors decreased from 5 to 4
- When node efl-1 was knocked down the number of attractors decreased from 5 to 3
- When node cki-1 was knocked down the cell cycle decreased from 8 time steps to 7 time steps.