Final project report + poster presentation: **Previous plan**

- Final report (regular sections similar to a research paper):
  - Abstract
  - Introduction
  - Data and Methods
  - Results & Discussion
  - Limitations & Future Directions
  - References
  - Glossary

Due

Fri, April 26

- Final poster presentation
  - All of you make posters.
  - Live poster session with peer evaluations.

Thr, April 30

12:45 – 2:45 pm

- Code & Results in a well-organized GitHub repository
  - Well-documented code download/process data, perform computational analyses, generate all the results including plots/tables)
  - Detailed documentation on how to run everything

Final project report + poster presentation: **New plan**

Here is my idea. This is NOT a mandate and, as always, I would like to hear what you think.

Final Project Report

- Let's try to keep the due date of Fri, Apr 26.
- **However**, if you need additional time, please let me know.
- Happy to accommodate your individual circumstances.

Final Poster Presentation:

I wish to give all of your the opportunity to make a poster about your awesome project, present it showcasing your effort, and cheer-for/evaluate each other's work.

Final project report + poster presentation: **New plan**

Here is my idea. This is NOT a mandate and, as always, I would like to hear what you think.

Final Poster Presentation

Before Thr, April 30

- Make your poster.
- Use zoom to record a 5 min video presenting it.
  - Submit your poster **PDF** and video **link** to me by 11:59 pm Tue, April 28.
- Just like the proposal peer-review set-up, I will pre-assign:
  - 2-3 peers to watch & evaluate each poster using a rubric that I will provide.
    - Submit completed evaluations to me as a PDF before 12pm Thr, Apr 30.
  - 2-3 peers to watch & prepare to ask Qs on Thr, Apr 30.
    - Submit your ≥2 questions to me as a PDF before 12pm Thr, Apr 30.

Final project report + poster presentation: **New plan**

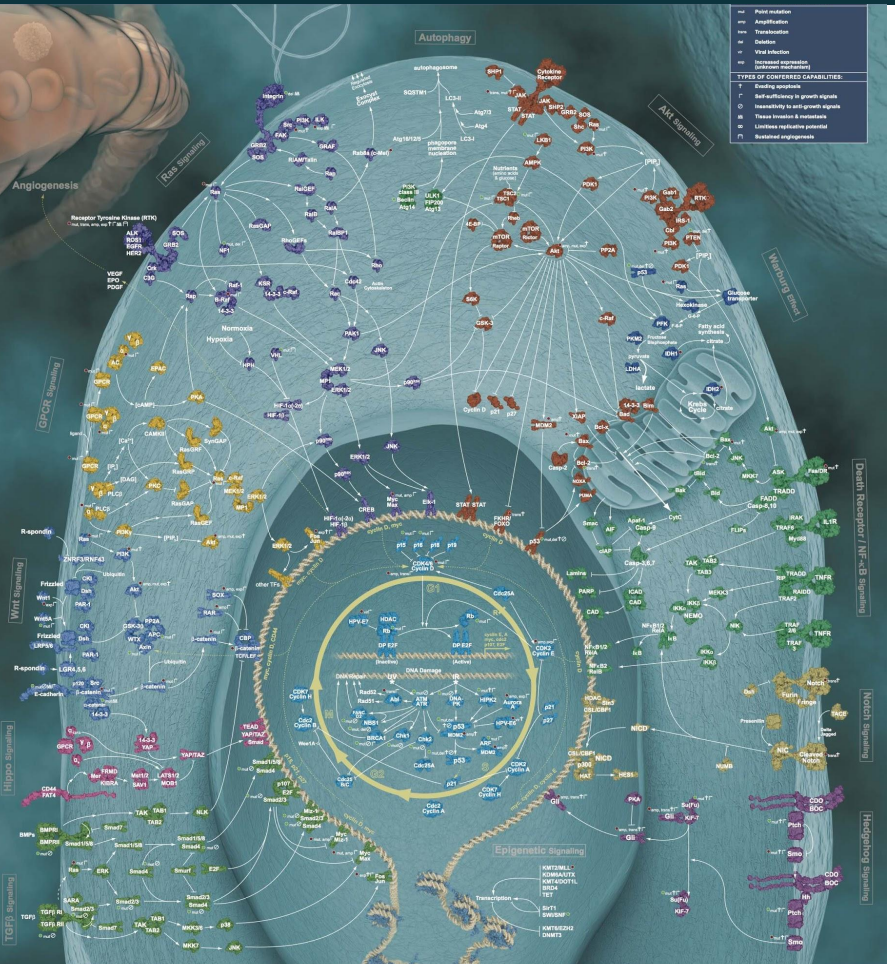
Here is my idea. This is NOT a mandate and, as always, I would like to hear what you think.

Final Poster Presentation

On Thr, April 30

- We'll do the following for each student:
  - **1 min** to give an overview of project.
    - I will share the poster PDF (to keep things going).
  - **2 min** to engage with the peer evaluators and question-askers.
    - I will call them out to talk.
  - **2 min** to engage with any other questions/comments from anyone.
    - Throughout, everyone can also ask questions & provide comments via chat.

Cellular signaling and regulatory pathways

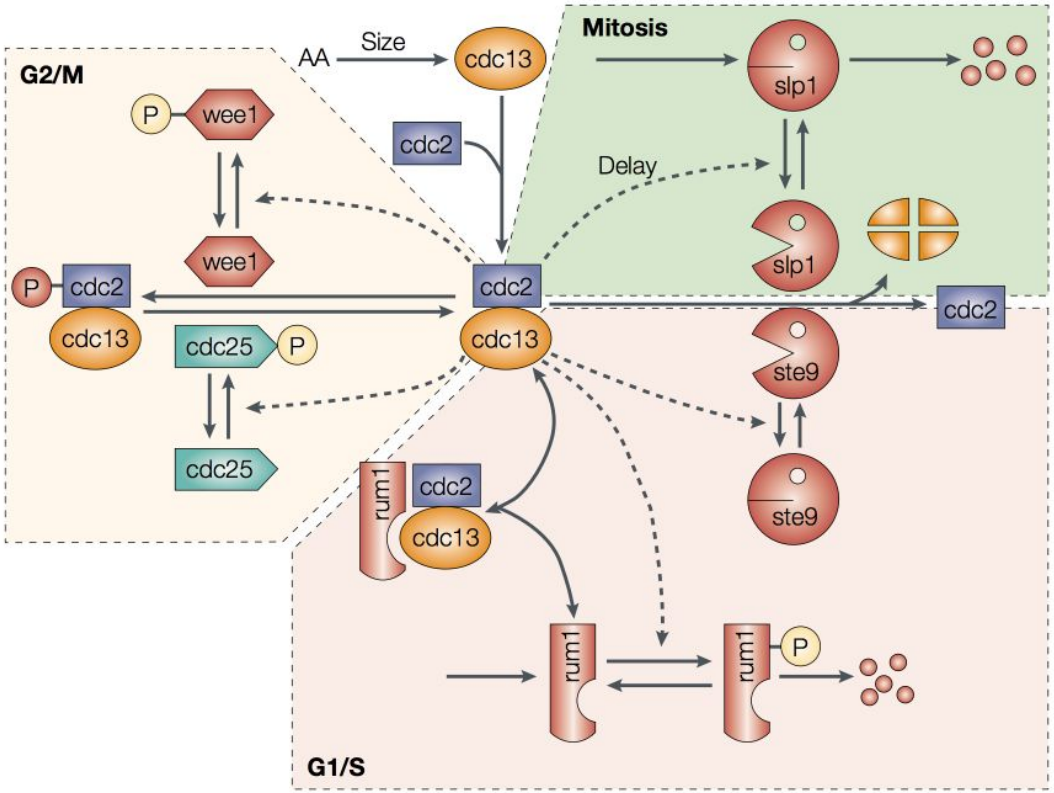


Cell physiology is governed by complex assemblies of interacting proteins carrying out most of the interesting jobs in a cell, such as metabolism, DNA synthesis, movement and information processing.

These processes are orchestrated by signaling and regulatory networks.

media.cellsignal.com

The cell-cycle control system in fission yeast

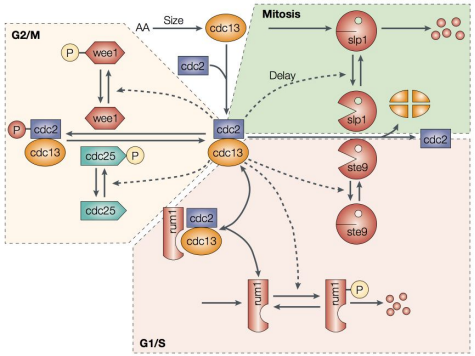


The cell cycle is divided into **phases** brought about by distinct signaling/regulatory interactions.

- **Brief G1 phase**: ste9 is active & rum1 is abundant.
- **Long S/G2 phase**: cdc2 is tyrosine phosphorylated
- Cell enters **M phase**: cdc25 removes the inhibitory phosphate group.
- After some delay, slp1 activates and degrades cdc13. As cdc2–cdc13 activity falls, the cell **exits mitosis**.
- Size decreases twofold at **nuclear division**.

Tyson (2001) Nat. Rev. Mol. Cel. Biol.

The cell-cycle control system is highly conserved



Fission yeast	Budding yeast	Frog egg	Mammal	Generic role
cdc2	Cdc28	Cdk1,2	Cdk1,2	Cyclin-dependent kinase
cdc13	Clb1–6	Cyclin A,B,E	Cyclin A,B,E	Cyclins
rum1	Sic1	Xic1	$p27^{Kip1}$	Stoichiometric inhibitor
ste9	Cdh1	Fizzy-related	Cdh1	APC auxiliary
slp1	Cdc20	Fizzy	$p55^{cdc}$	APC auxiliary
wee1	Swe1	Wee1	Wee1	Tyrosine kinase
cdc25	Mih1	Cdc25C	Cdc25C	Tyrosine phosphatase

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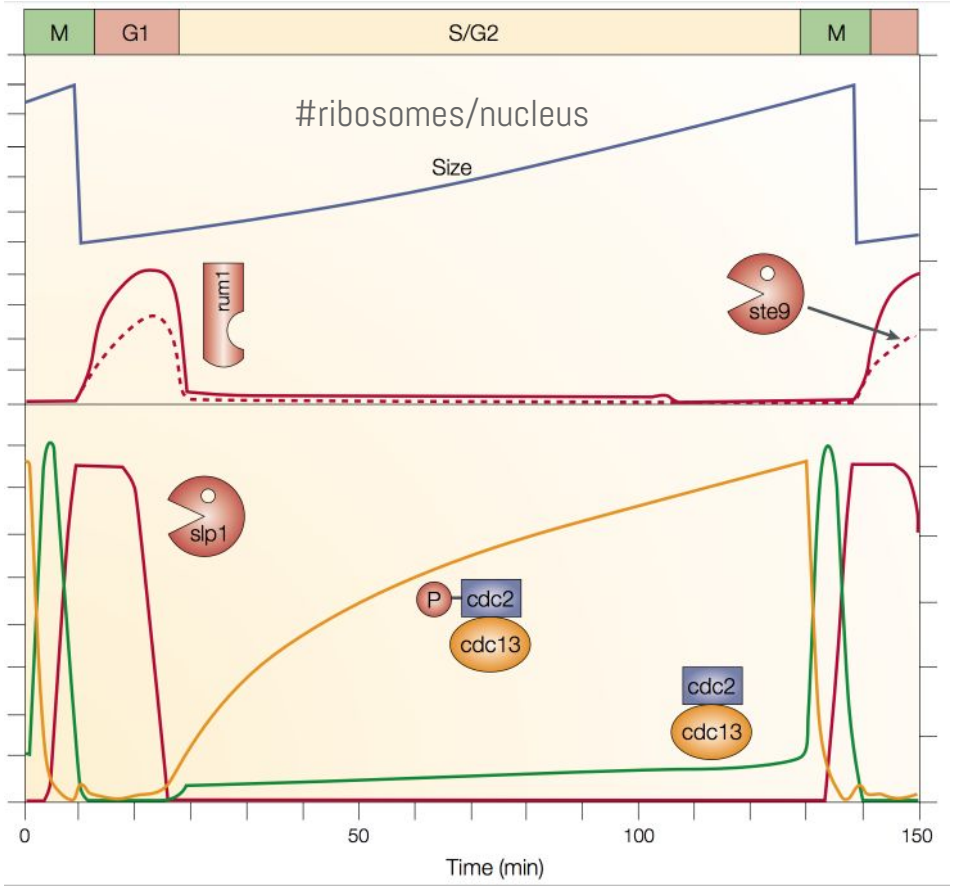
Modeling the cell-cycle control system in fission yeast



Write the full set of differential equations that describe the wiring diagram.

Perform numerical integration of these equations to get time courses.

- Brief G1 phase: ste9 is active & rum1 is abundant.
- Long S/G2 phase: cdc2 is tyrosine phosphorylated
- Cell enters M phase: cdc25 removes the inhibitory phosphate group.
- After some delay, slp1 activates and degrades cdc13. As cdc2–cdc13 activity falls, the cell exits mitosis.
- Size decreases twofold at nuclear division.

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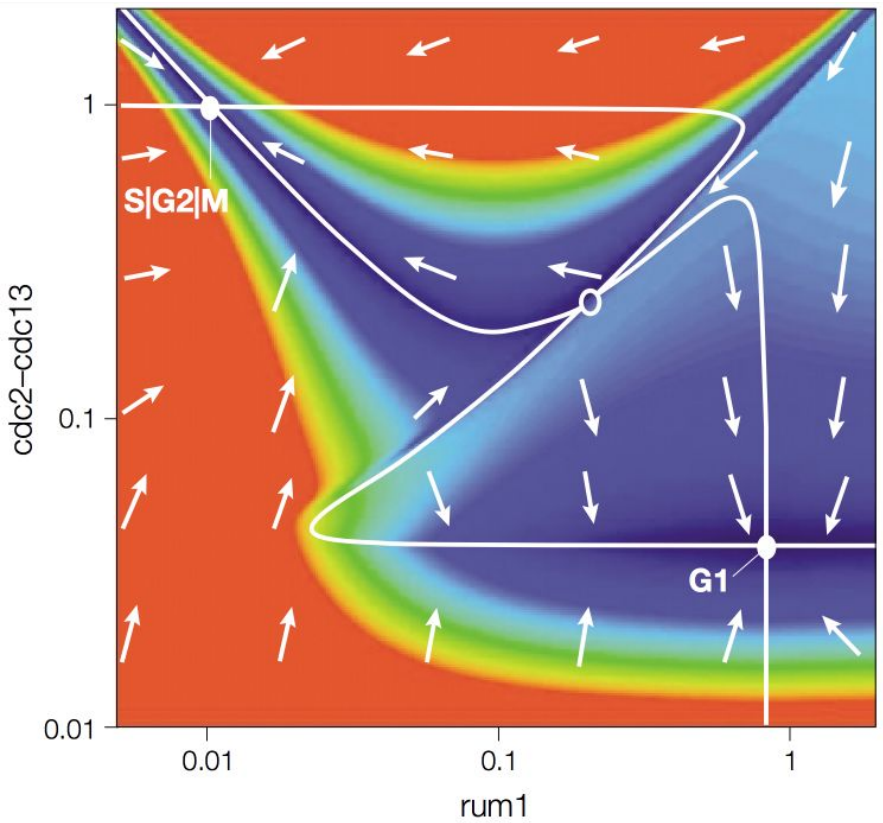
State spaces and vector fields

At any given point, the differential equations determine how fast the state of the system is changing.

Let's consider the rates of change of [cdc2–cdc13] and [rum1].

- Plot [rum1] vs. [cdc2–cdc13].
- We know the equations d[rum1]/dt and d[cdc2–cdc13]/dt.
- Each point in this space is associated with an arrow, which indicates the direction and magnitude of the rates of change of [cdc2–cdc13] and [rum1].

The collection of arrows at every point in **state space** defines the **vector field** of the dynamical system.

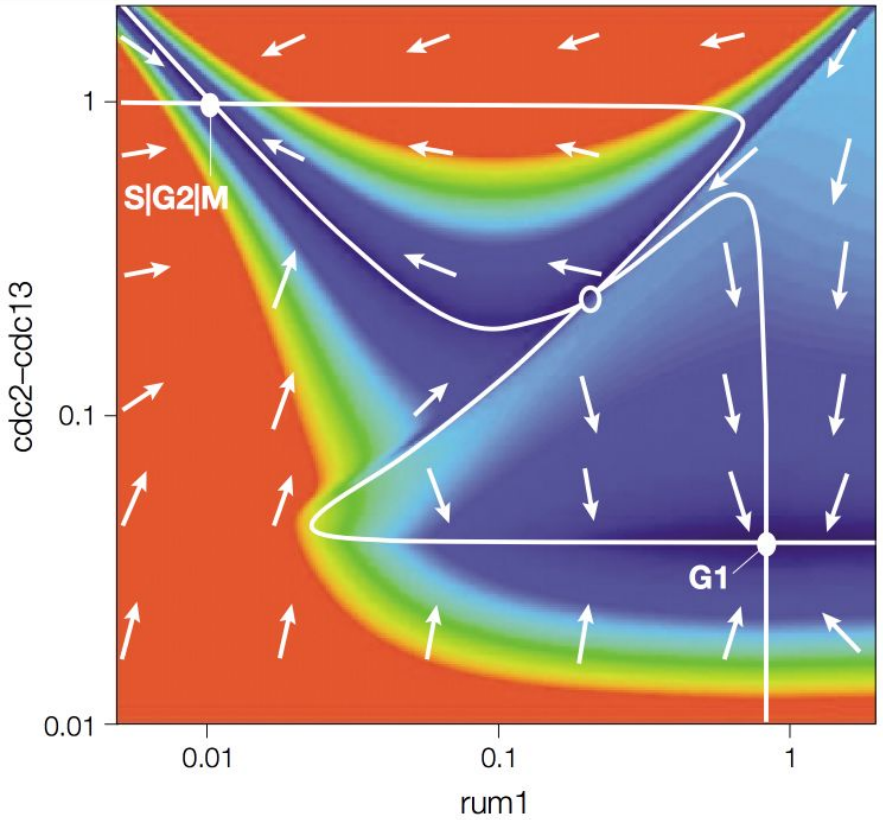


Tyson (2001) Nat. Rev. Mol. Cel. Biol.

State spaces and vector fields

We know the eqs d[rum1]/dt & d[cdc2–cdc13]/dt.

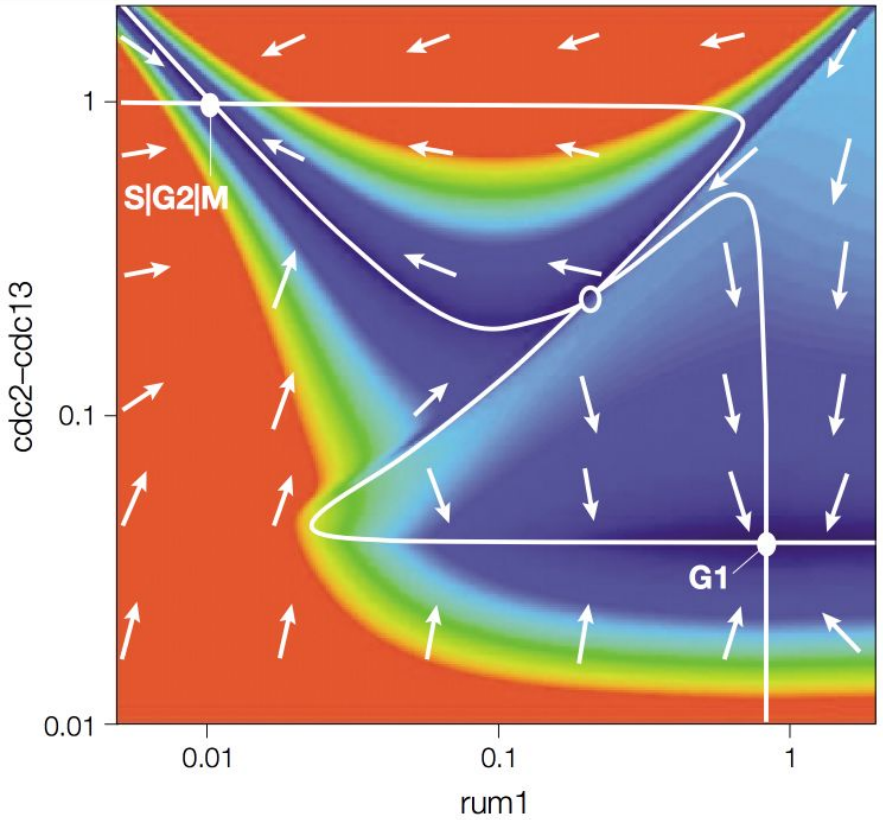
- Solve d[rum1]/dt = 0.
  - Returns a curve that represents all the points in the state space where [rum1] does not change (steady state).
  - All vectors on this curve are vertical.
- Solve d[cdc2–cdc13]/dt = 0.
  - Returns a curve that represents all the points in the state space where [cdc2–cdc13] does not change.
  - All vectors on this curve are horizontal.
- These two curves are called the **nullclines**.
- Add these curves to the state space.



Tyson (2001) Nat. Rev. Mol. Cel. Biol.

State spaces and vector fields

- The collection of arrows at every point in **state space** defines the **vector field** of the dynamical system.
- A plot of two variables displaying the vector field and the nullclines is called the **phase plane**.
    - Direction of the vectors: arrow
    - Magnitude of the vectors: color (red, fast; blue, slow).
    - Curves: nullclines with horizontal/vertical vectors.
    - Within the regions bounded by these curves, all arrows lie in the same quadrant of compass directions.



Tyson (2001) Nat. Rev. Mol. Cel. Biol.

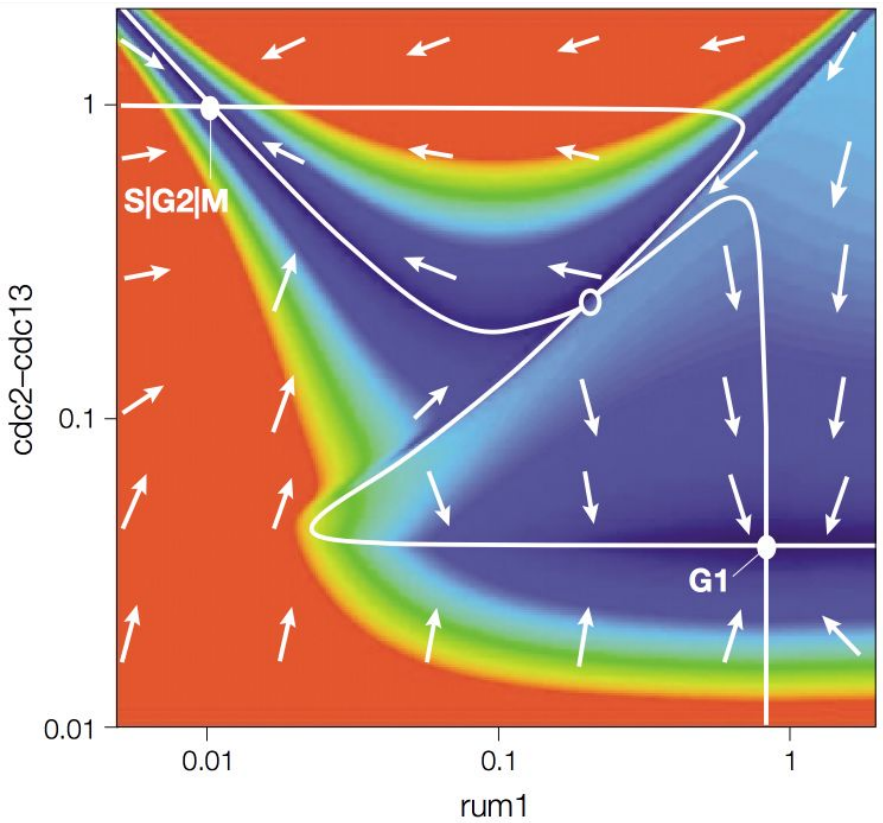
State spaces and vector fields

Knowing the vector field, one can predict the response of the control system to any initial condition - simply pick a starting point and follow the arrows.

In this case, the dynamical system has two attractors (●); in the vicinity of a stable steady state, all arrows point towards the steady state.

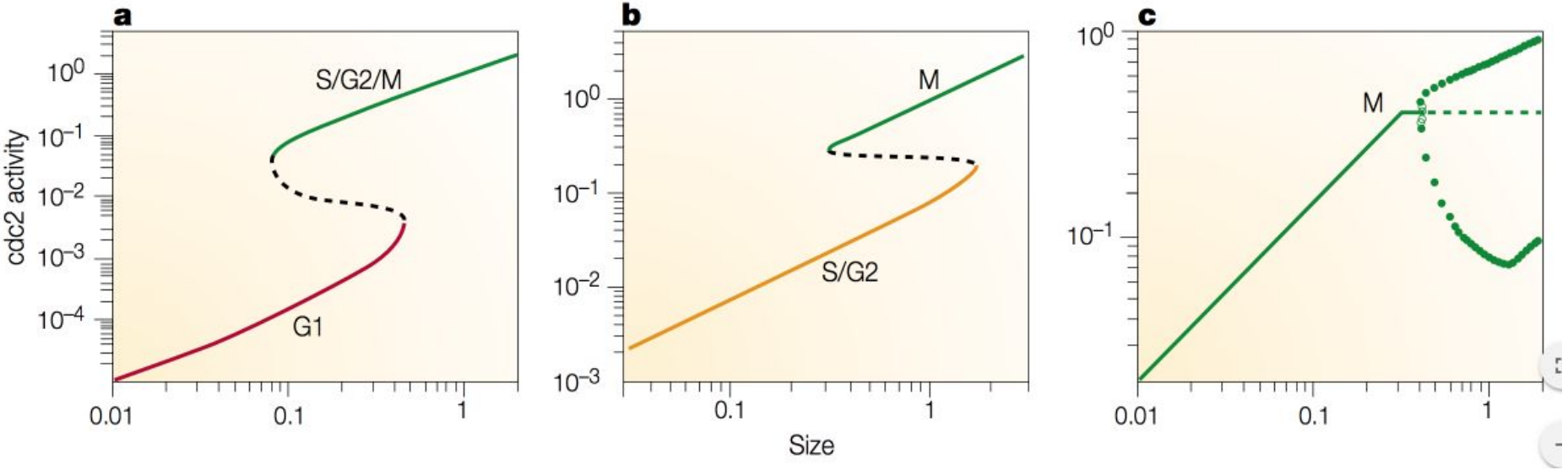
The intermediate steady state (o) is an unstable saddle point (attractive in two directions and repelling in all others).

The 'state-space' idea is readily generalized to any number of dynamical variables, but the vector field is hard to visualize in 3 or more dimensional state space.



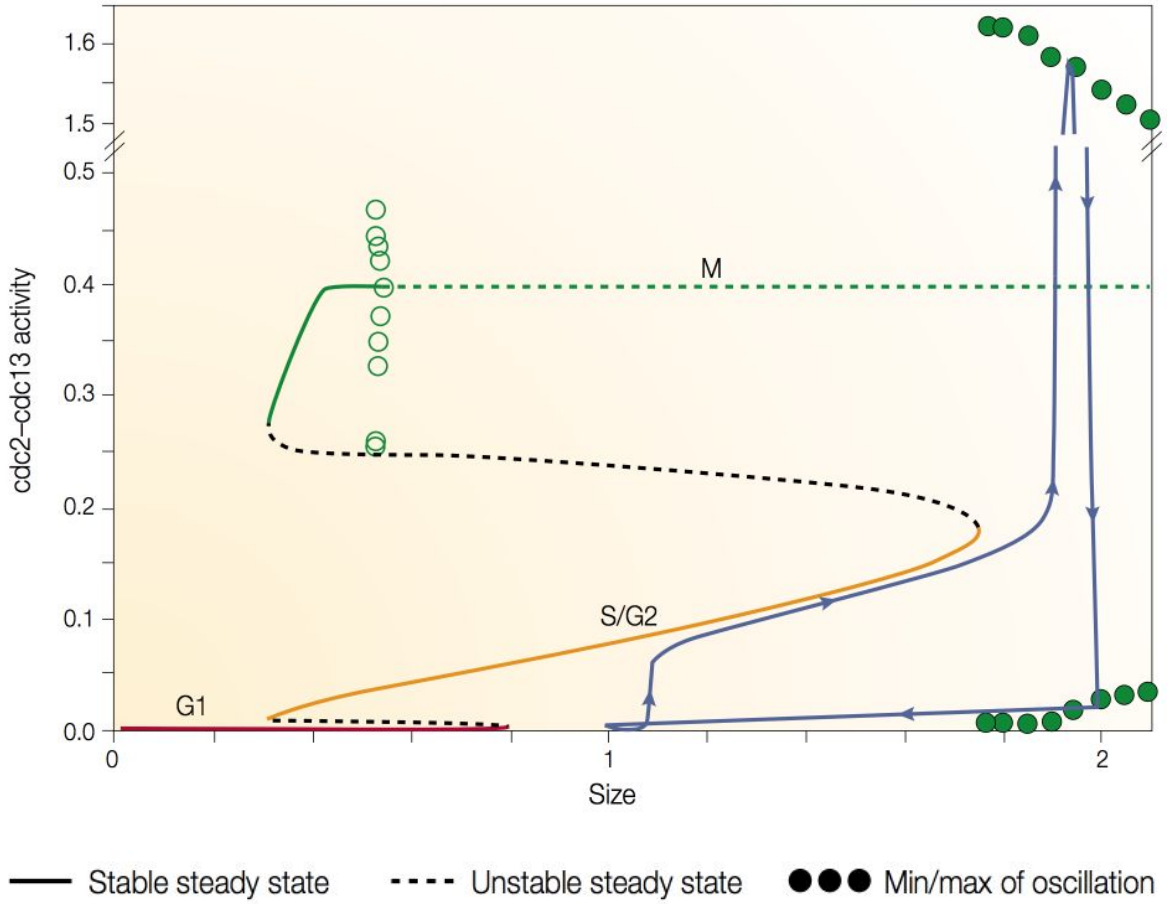
Tyson (2001) Nat. Rev. Mol. Cel. Biol.

Bifurcation diagrams for the three control modules of the cell cycle



Tyson (2001) Nat. Rev. Mol. Cel. Biol.

Bifurcation diagram for the full cell-cycle control network



Composite of the 3 diagrams: not a simple sum of the bifurcation diagrams of modules. (e.g. oscillations around the M state)

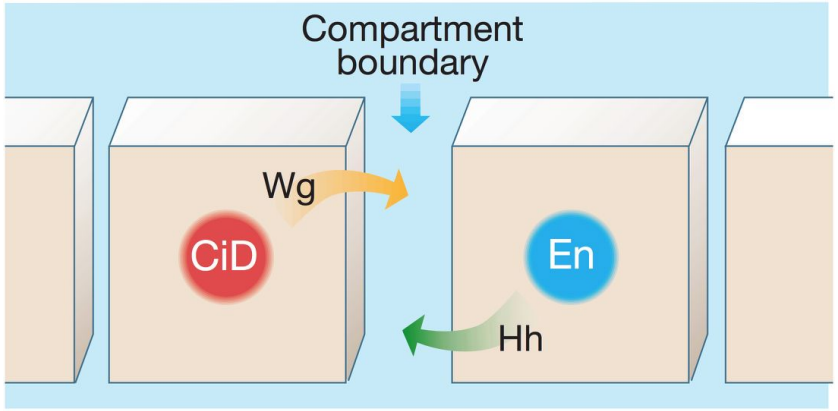
Blue line: Cell-cycle orbit from time course data.

At small cell size, all three modules support stable steady states.

The cell-cycle orbit follows the attractors of the control system.

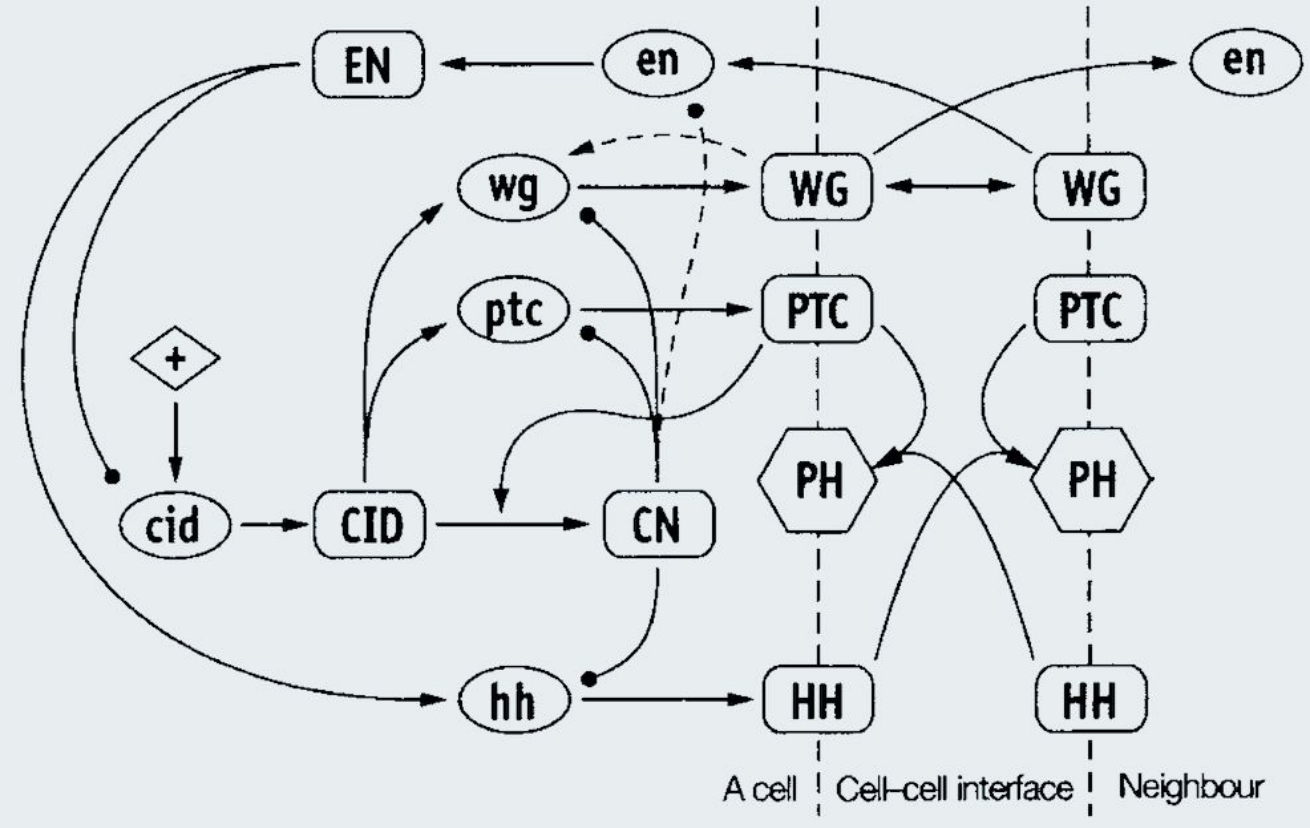
Tyson (2001) Nat. Rev. Mol. Cel. Biol.

Modeling segment polarity



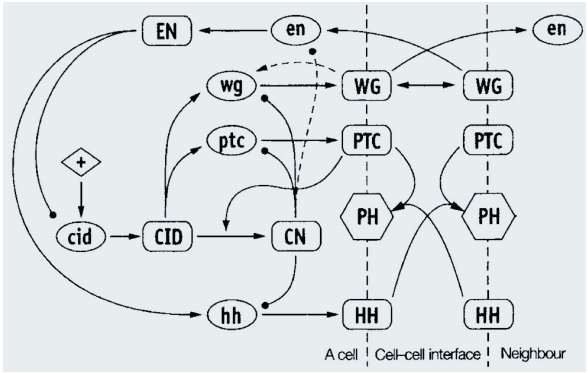
Dearden, Akam (2000) Nat.

Modeling segment polarity



Von Dassow (2000) Nat.

Modeling segment polarity



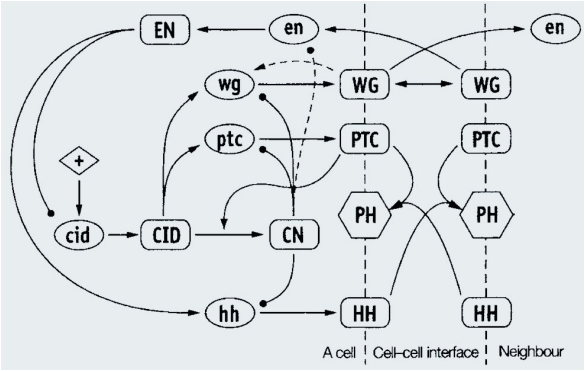
$$\frac{d[hh]_i}{dt} = T_{\max}\rho_{hh}\left[\frac{[EN]_i^{\nu_{ENhh}}}{K_{ENhh}^{\nu_{ENhh}} + [EN]_i^{\nu_{ENhh}}}\right] - \frac{[hh]_i}{H_{hh}}$$

$$\frac{d[HH]_{i,j}}{dt} = \frac{P_{\max}\sigma_{HH}[hh]_i}{6} - \frac{[HH]_{i,j}}{H_{HH}} - k_{PTCHH}[HH]_{i,j}[PTC]_{n,j+3}$$

$$\frac{d[PH]_{i,j}}{dt} = k_{PTCHH}[HH]_{n,j+3}[PTC]_{i,j} - \frac{[PH]_{i,j}}{H_{PH}}$$

Von Dassow (2000) Nat.

Modeling segment polarity



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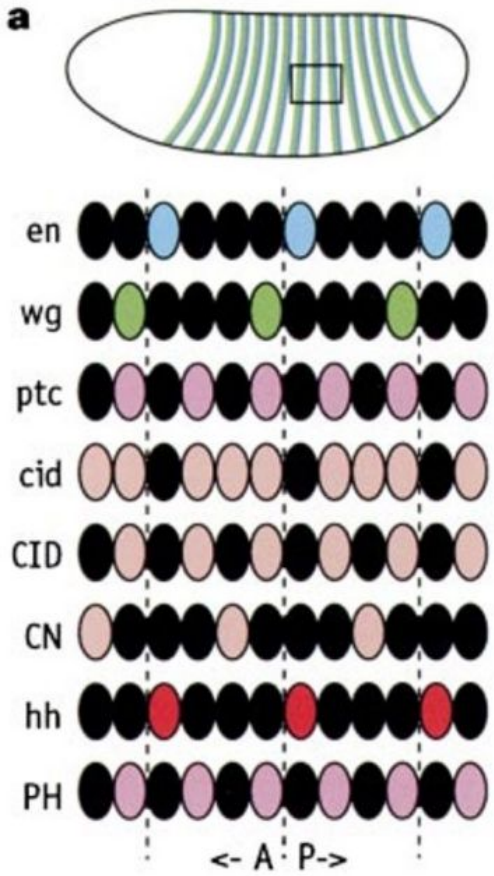
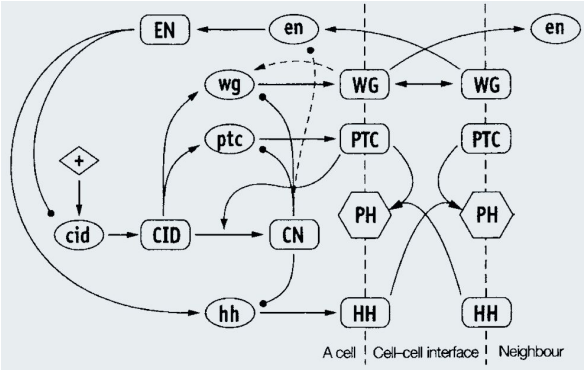


Von Dassow (2000) Nat.

Modeling segment polarity



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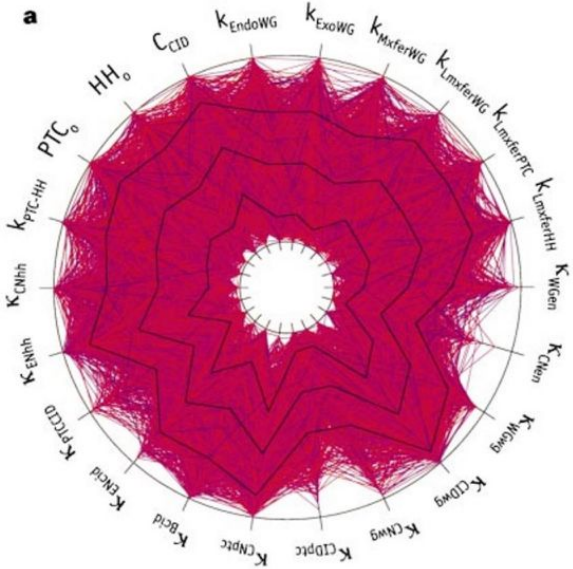

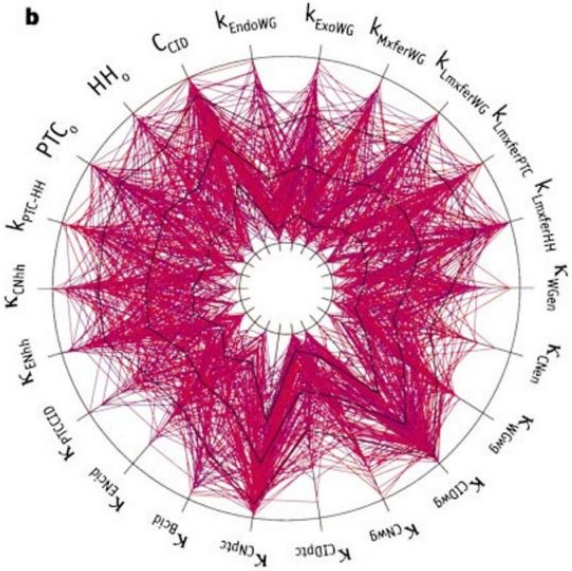

Von Dassow (2000) Nat.

Broad ideas

Kinetic modelling and bifurcation theory provide a precise, mathematical connection between the molecular networks and cellular physiology.

Can be used to make powerful predictions.

Several modeling strategies:

- Rate equations
- Boolean (& hybrid) modeling
- Stochastic simulations