

# Models and mechanism

- Keystone goal: **Prediction** ("What would happen if...")

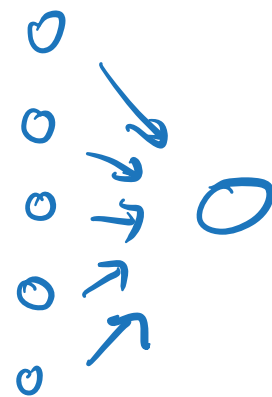
if **A** is increased, then...



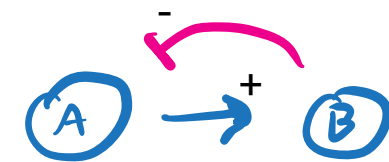
- Keystone challenge: Biological systems are **complex** (not just big)



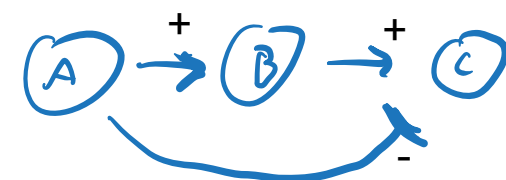
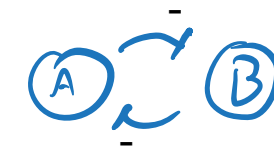
not complex



not complex

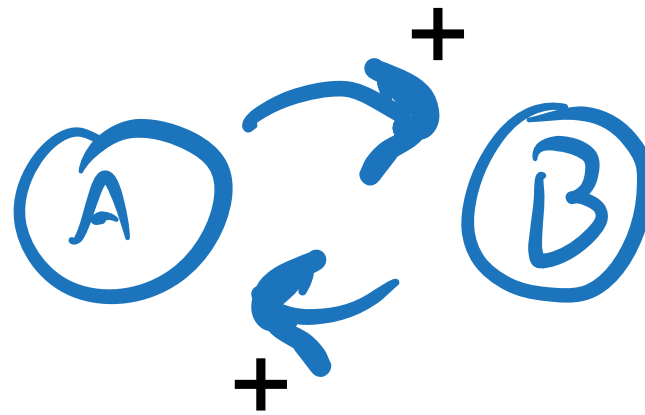


complex!



- Keystone tool: Dynamical systems, control theory, (the differential equation,) ...

stress

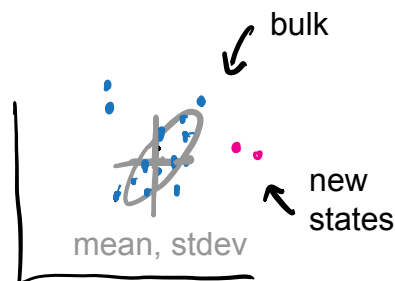


breathing  
rate

# the goals, challenges, systems, tools and approaches of today

## Data and analytics

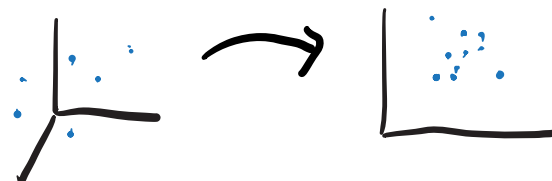
- Keystone goal: **Discover the hidden** (new states, cell types, disease classes,...)



- Keystone challenge: Biological data is not just big, it's **high-dimensional**.

30000 genes  
1000 cells

$10^4$  microbial species  
20 patients



- Keystone tool: Clustering, regression, dimension-reduction... coding

## Models and mechanism

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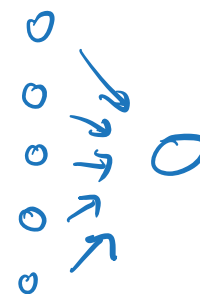
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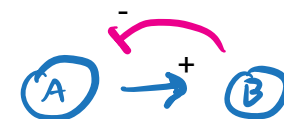
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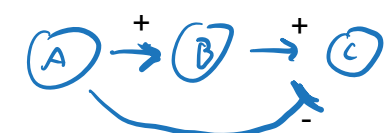
not complex



not complex



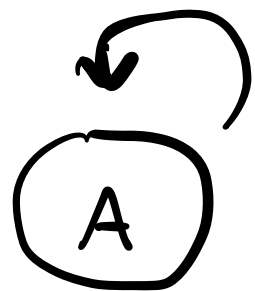
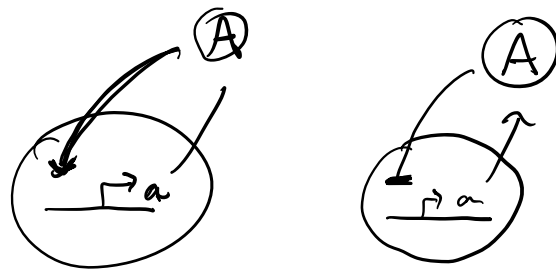
complex!



- Keystone tool: Dynamical systems, control theory, (the differential equation,) ...

# Complex biological systems and “systems thinking”

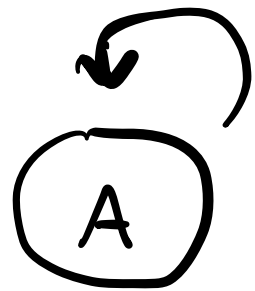
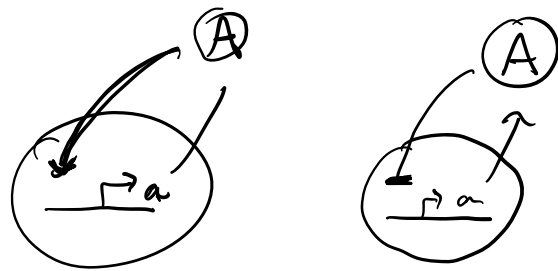
→ Activation  
⊥ Repression



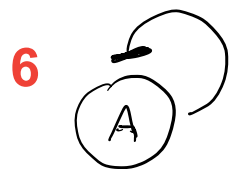
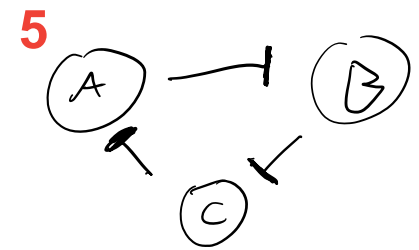
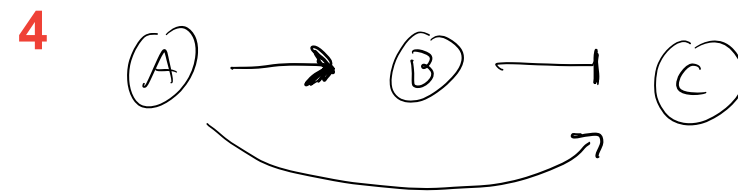
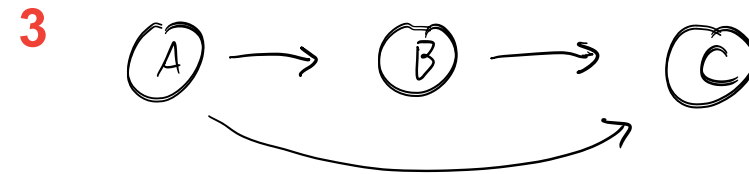
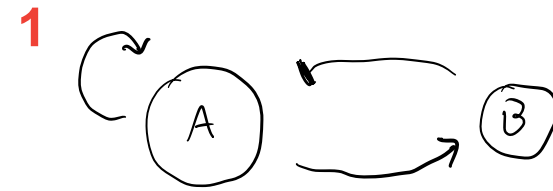
Positive feedback

- With positive feedback, the curve showing steady-state protein as a function of activator TF should move up.
- Does the curve move up by:
  - Shifting the EC50 to the left?
  - Moving up at high-C?
  - Moving up at low-C?
  - Combination of all 3?

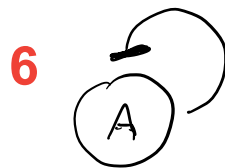
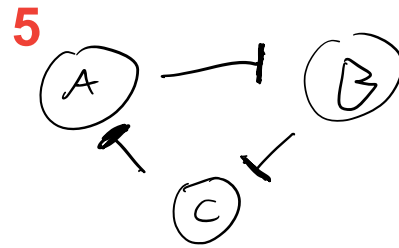
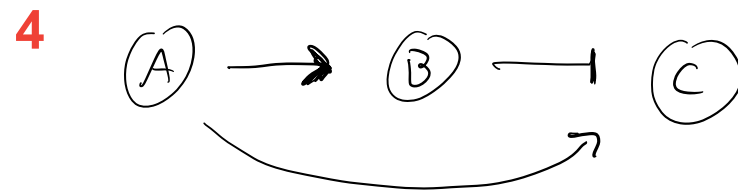
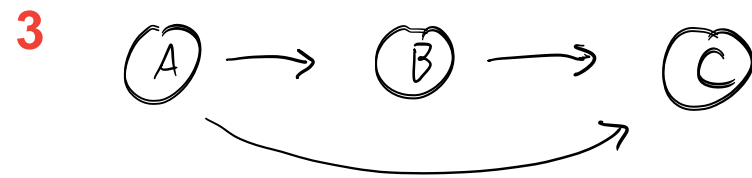
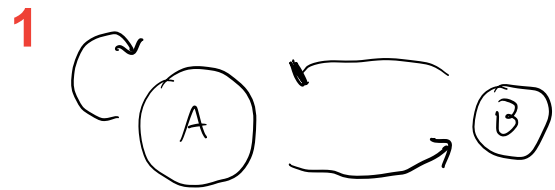
→ Activation  
 T Repression



Positive feedback



# In-class activity: Matching



- Direct negative feedback
- Indirect negative feedback
- Double-negative feedback
- Fast positive and slow negative feedback
- Incoherent feedforward
- Coherent feedforward
- The Repressilator