

# Representation, Learning and Inference in Models of Cellular Networks

BMI/CS 576

[www.biostat.wisc.edu/bmi576/](http://www.biostat.wisc.edu/bmi576/)

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# Various Subnetworks within Cells

- *metabolic*: describe reactions through which enzymes convert substrates to products
- *regulatory* (genetic): describe interactions that control expression of particular genes
- *signaling*: describe interactions among proteins and (sometimes) small molecules that relay signals from outside the cell to the nucleus
- note: these networks are linked together and the boundaries among them are not crisp





# A Signaling Network

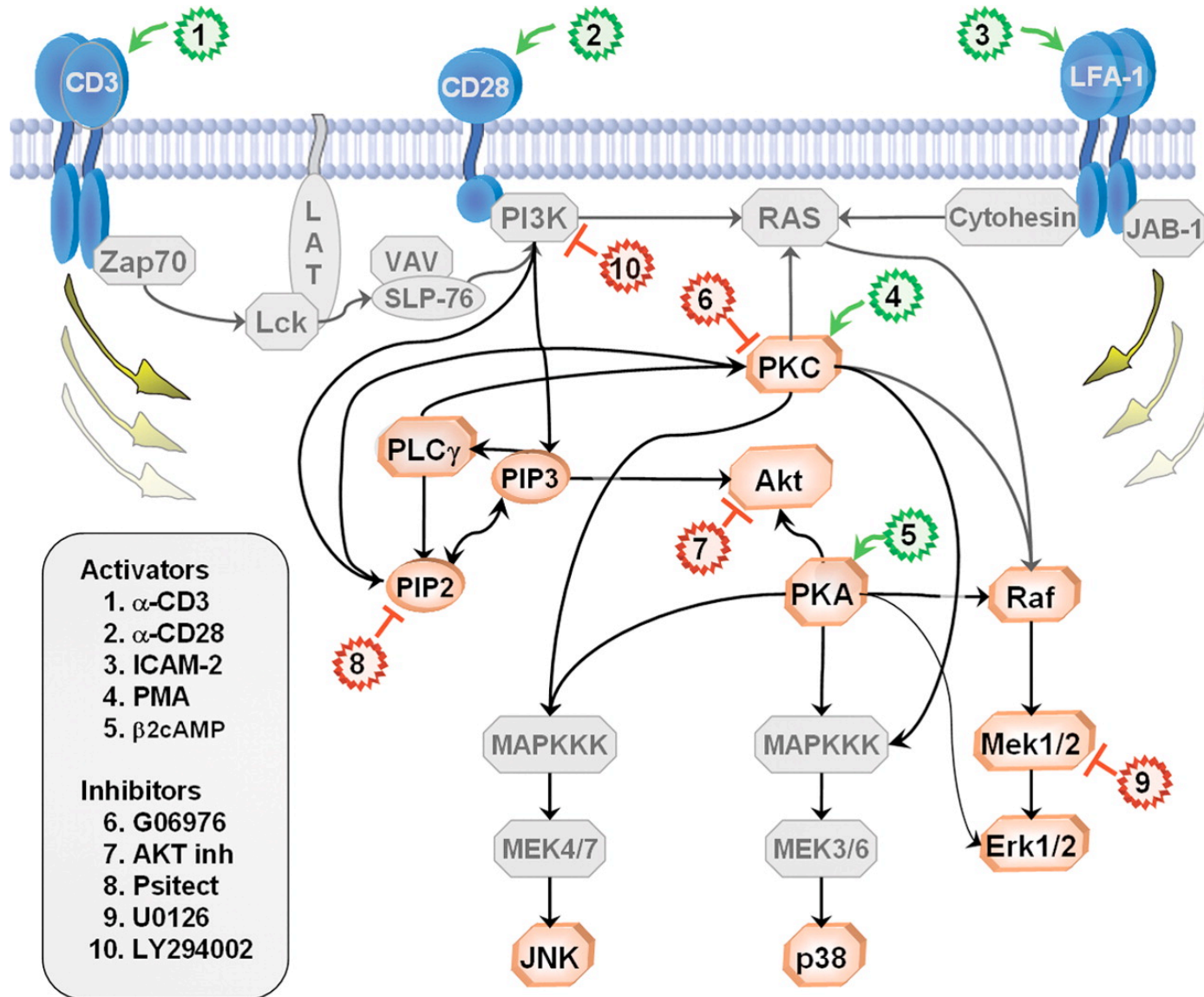


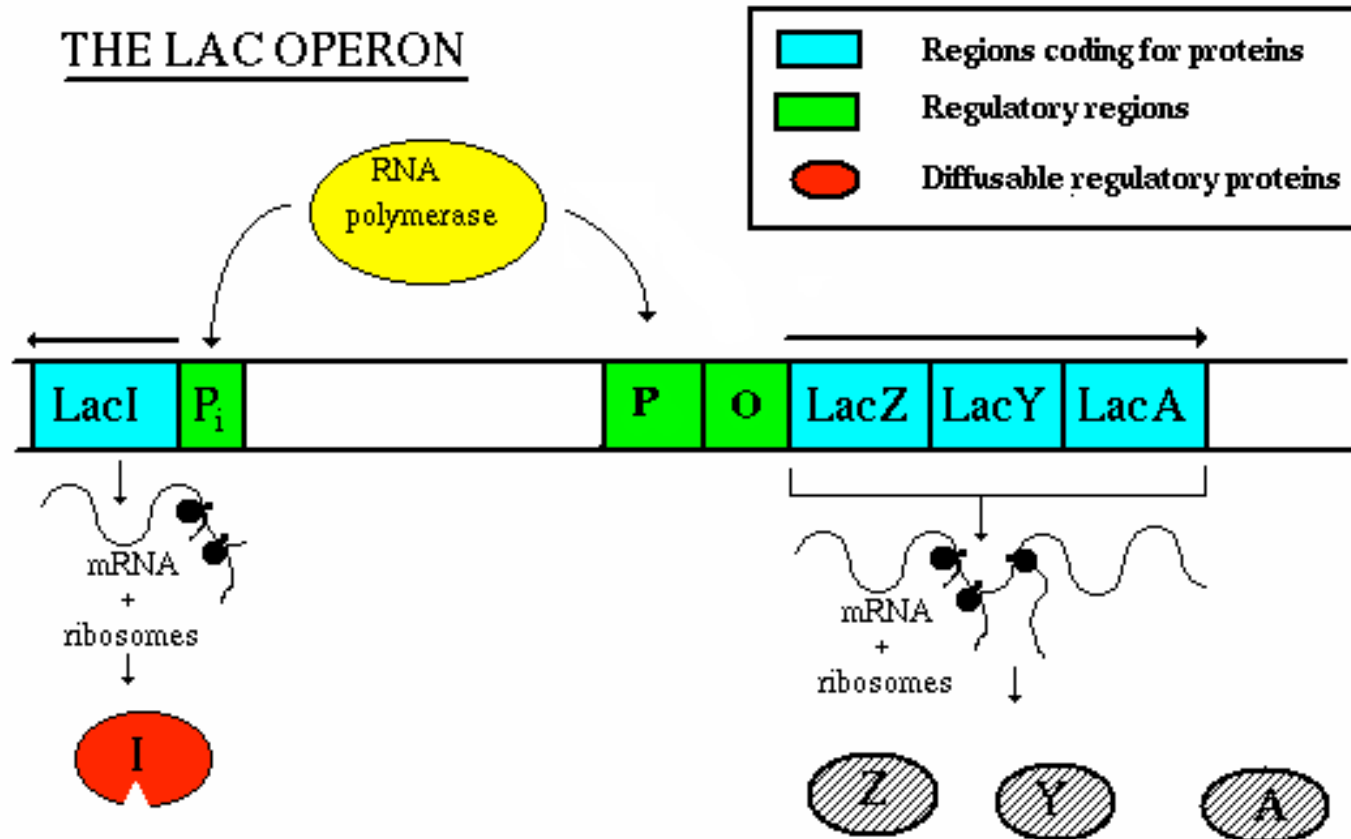
Figure from Sachs et al., *Science* 2005

# Two Key Tasks

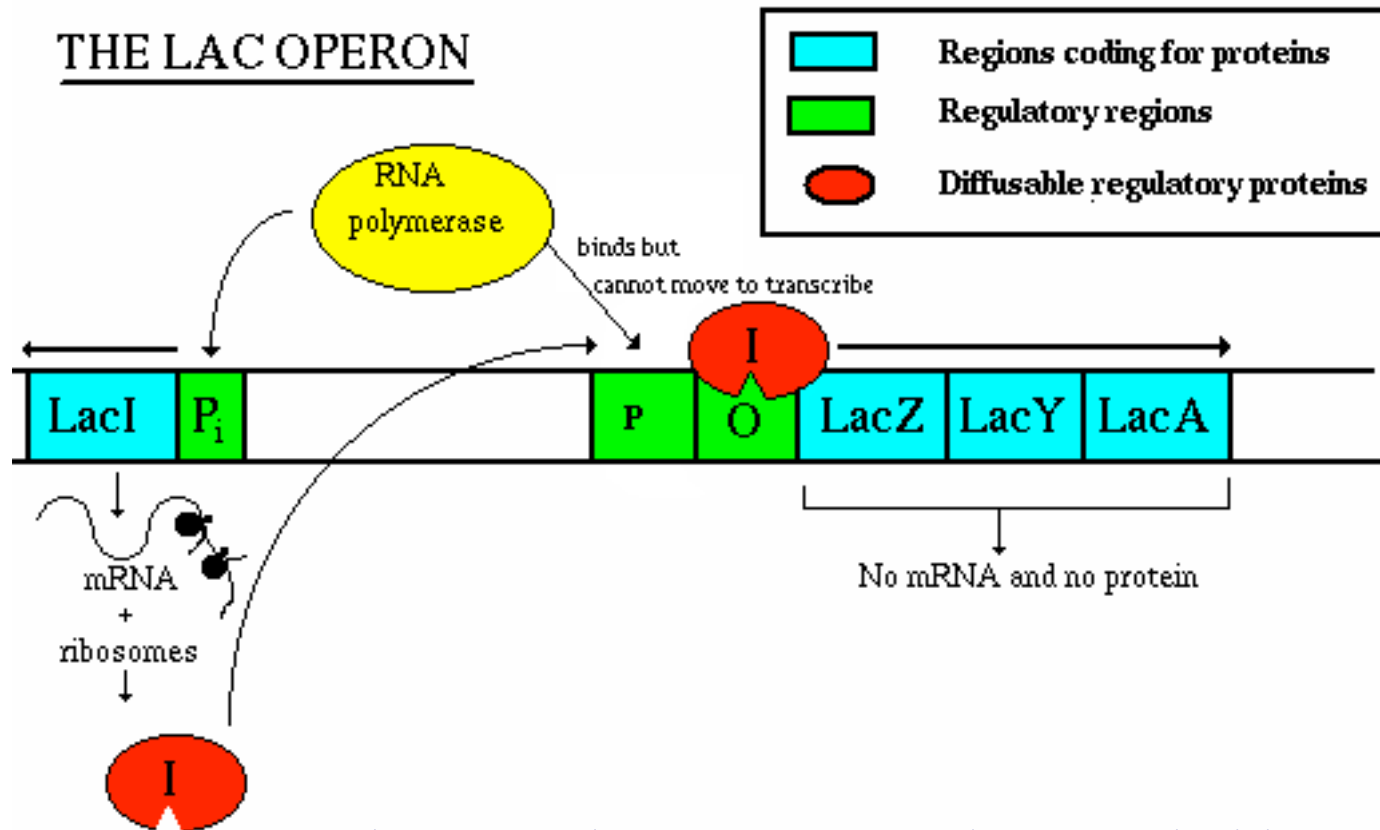
- *learning*: given background knowledge and high-throughput data, try to infer the (partial) structure/parameters of a network
- *inference*: given a (partial) network model, use it to predict an outcome of biological interest (e.g. will the cells grow faster in medium  $x$  or medium  $y$ ?)
- both of these are challenging tasks because typically
  - data are noisy
  - data are incomplete – characterize a limited range of conditions
  - important aspects of the system not measured – some unknown structure and/or parameters

# Transcriptional Regulation Example: the lac Operon in *E. coli*

*E. coli* can use lactose as an energy source, but it prefers glucose. How does it switch on its lactose-metabolizing genes?

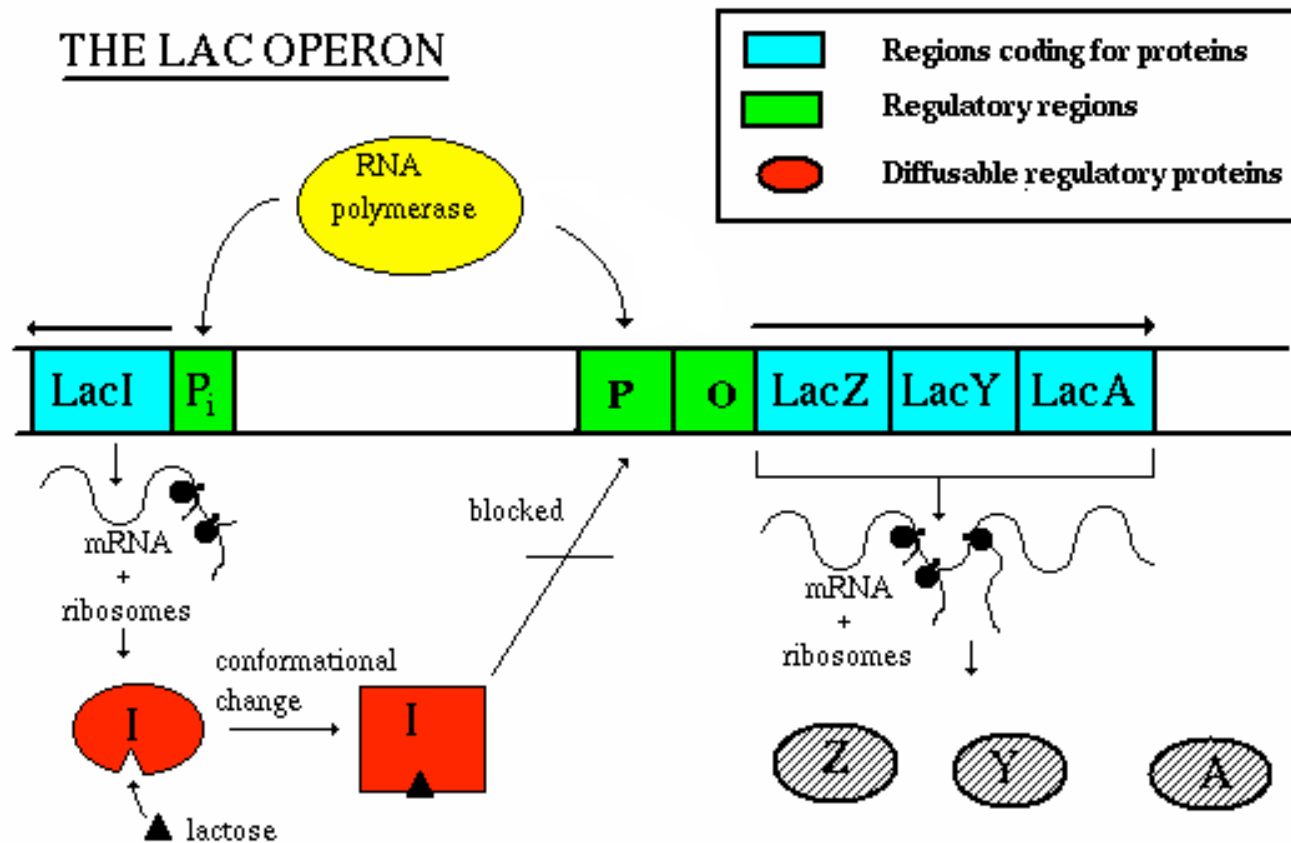


# The lac Operon: Repression by LacI



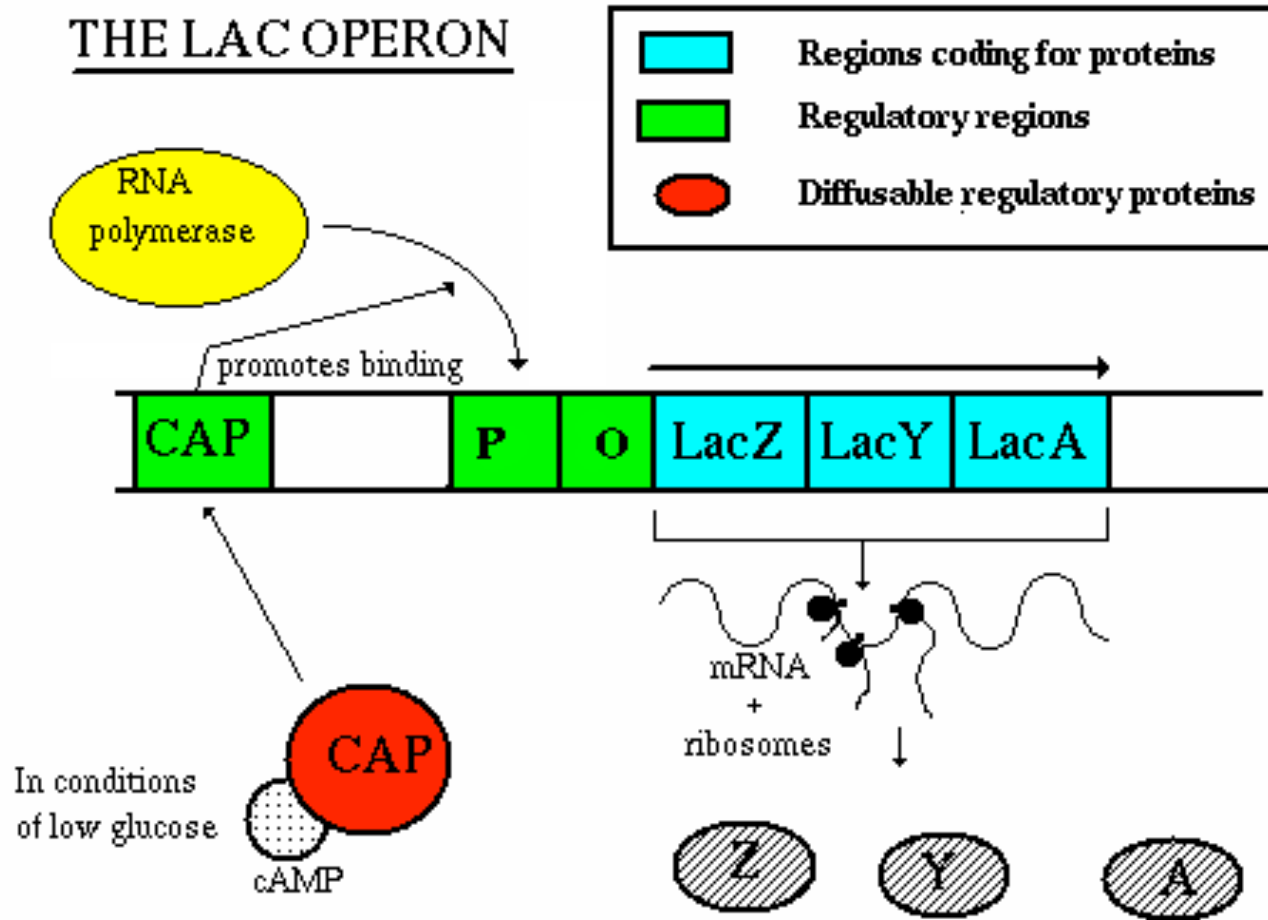
lactose absent  $\Rightarrow$  protein encoded by lacI represses transcription of the lac operon

# The lac Operon: Induction by LacI



lactose present  $\Rightarrow$  protein encoded by lacI won't bind to the operator (O) region

# The lac Operon: Activation by Glucose



glucose absent  $\Rightarrow$  CAP protein promotes binding by RNA polymerase; increases transcription

# Network Model Representations

- directed graphs
- Boolean networks
- differential equations
- ✓ Bayesian networks and related graphical models
- etc.