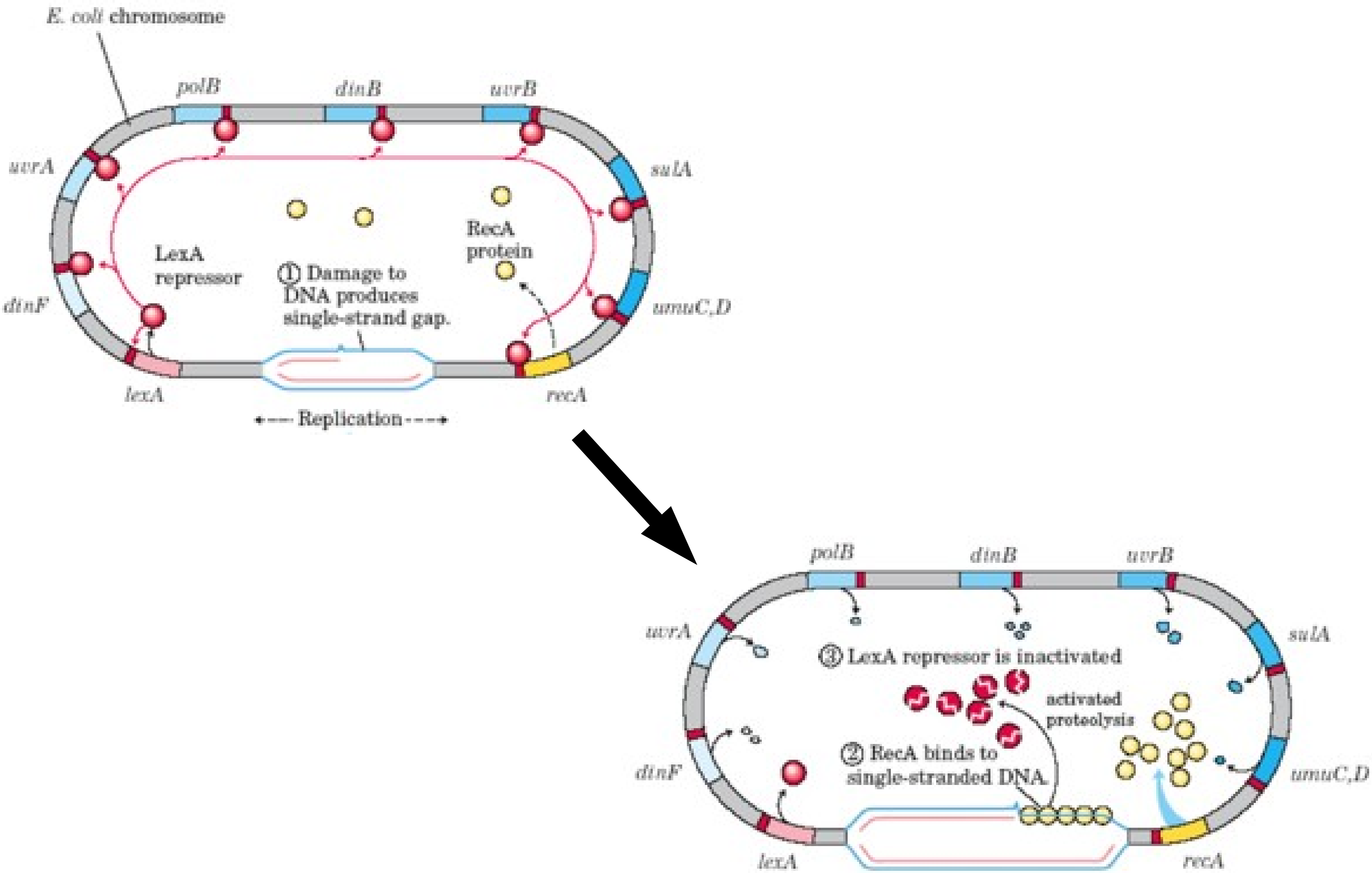
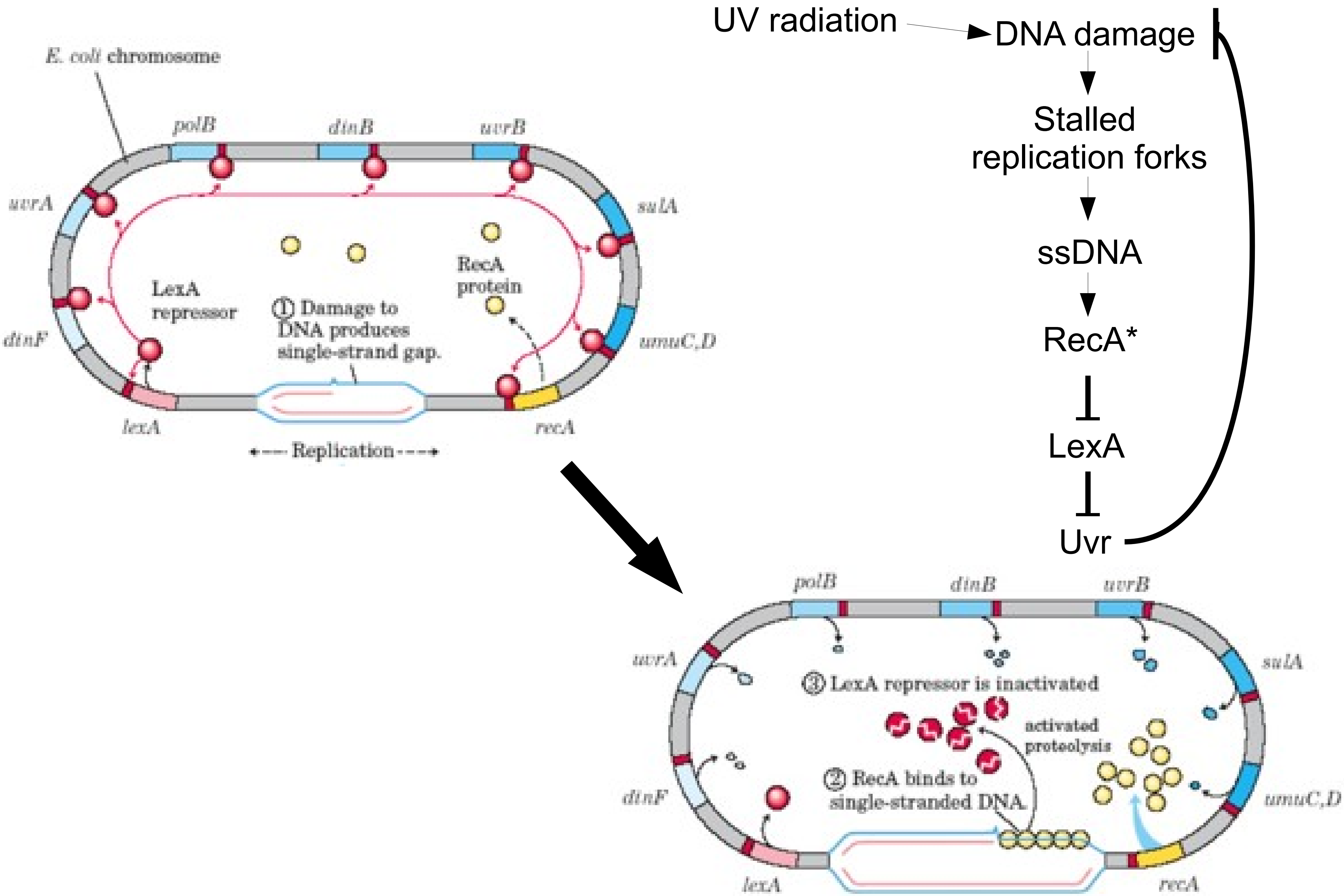
Negative Feedback

SOS response to DNA damage in E. coli



http://2012hs.igem.org/Team:Heidelberg_LSL/Project_SOS

SOS response to DNA damage in E. coli



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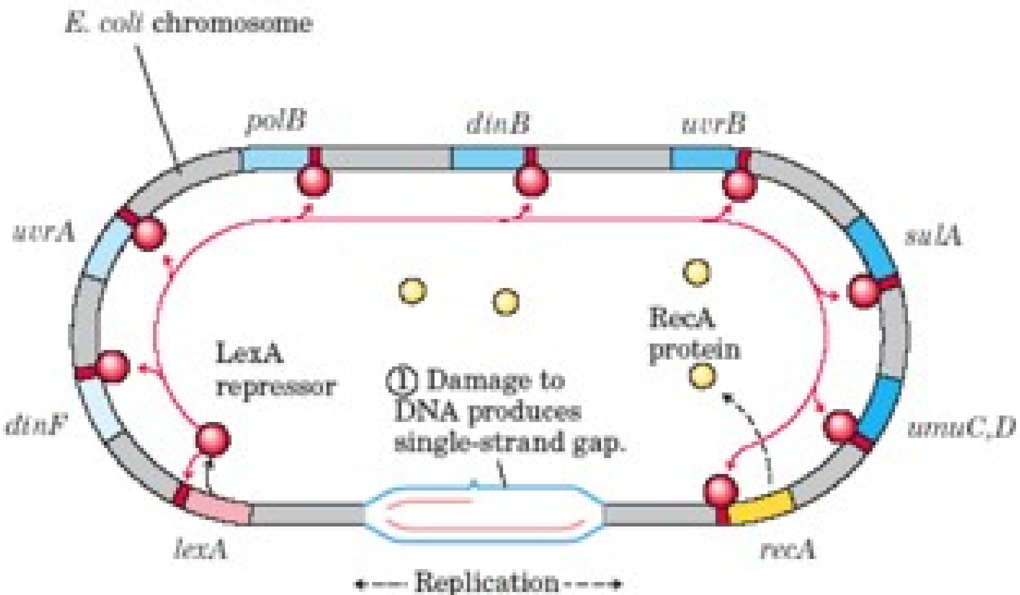
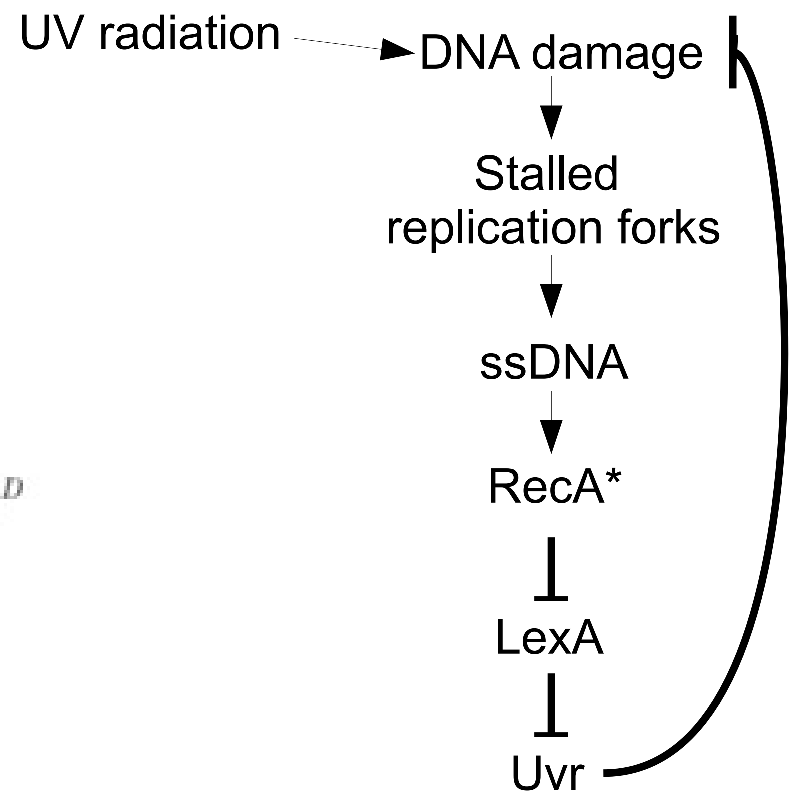
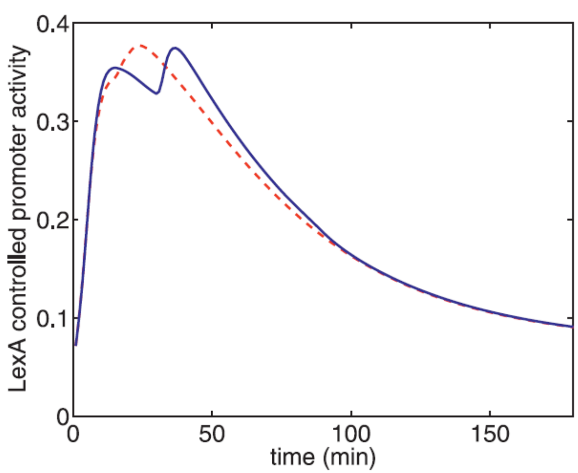
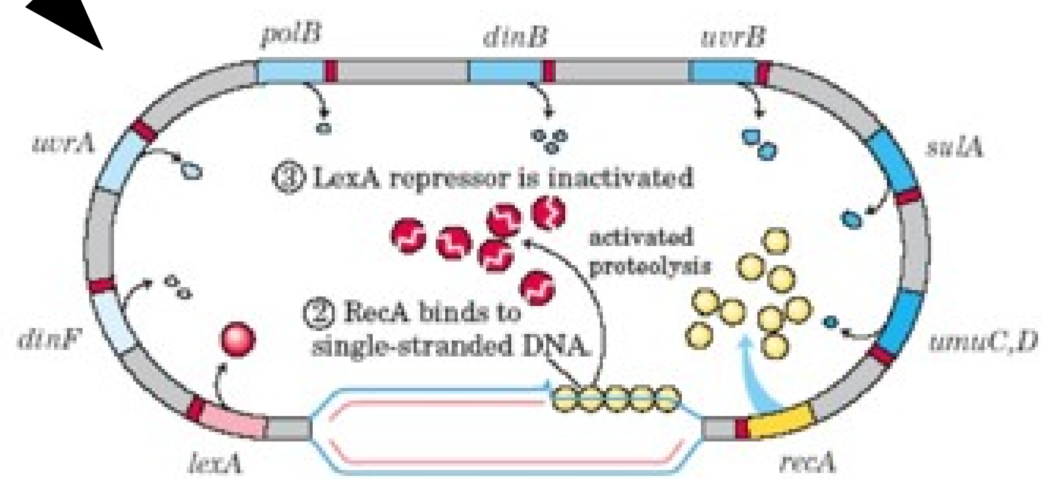
SOS response to DNA damage in E. coli





Net result of negative feedback: Homeostasis





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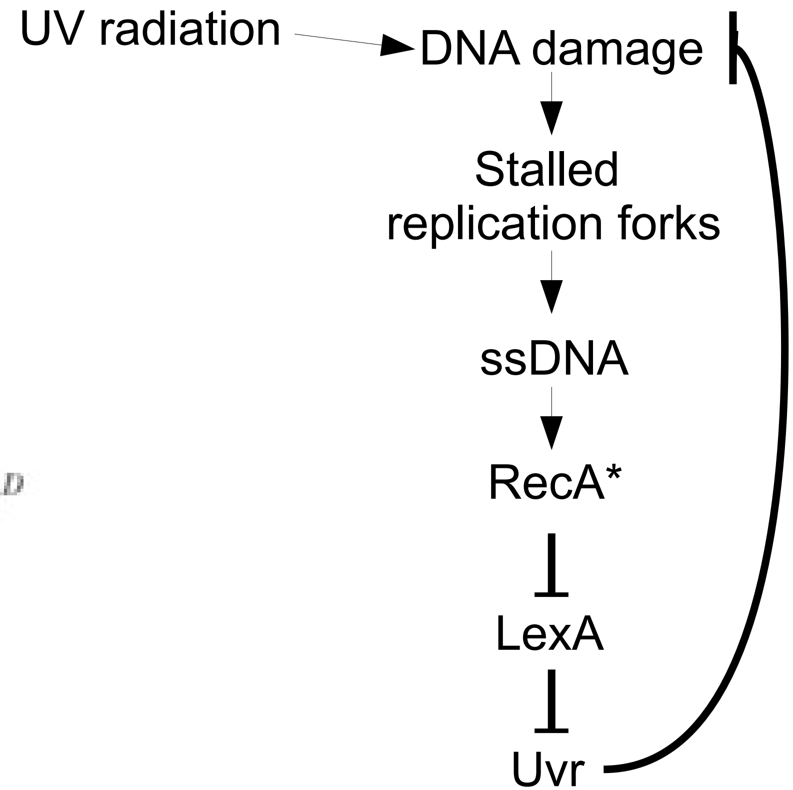
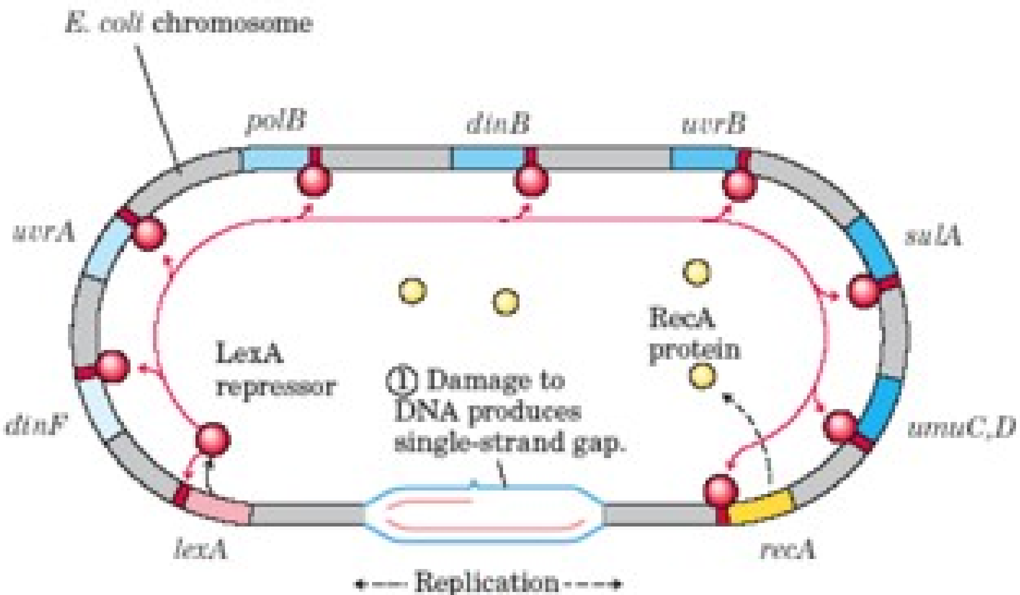
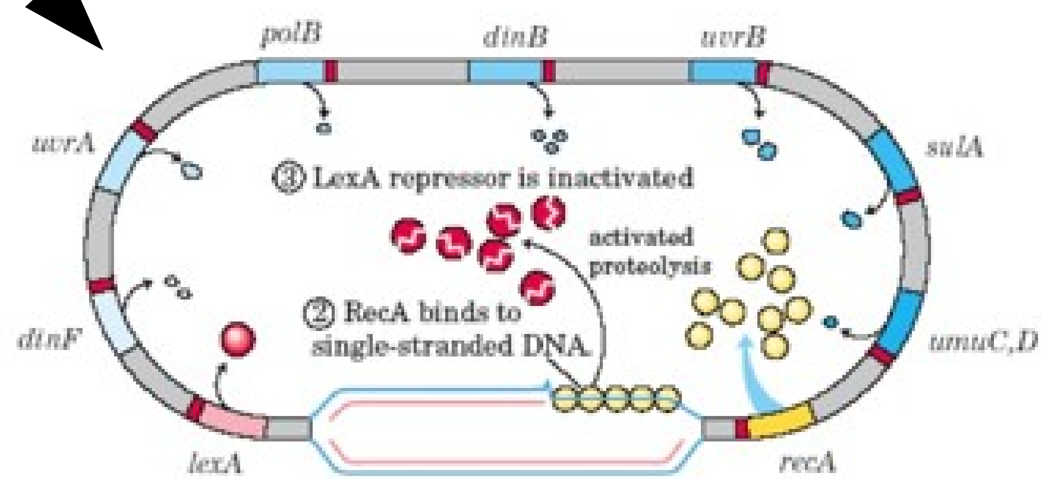
SOS response to DNA damage in E. coli







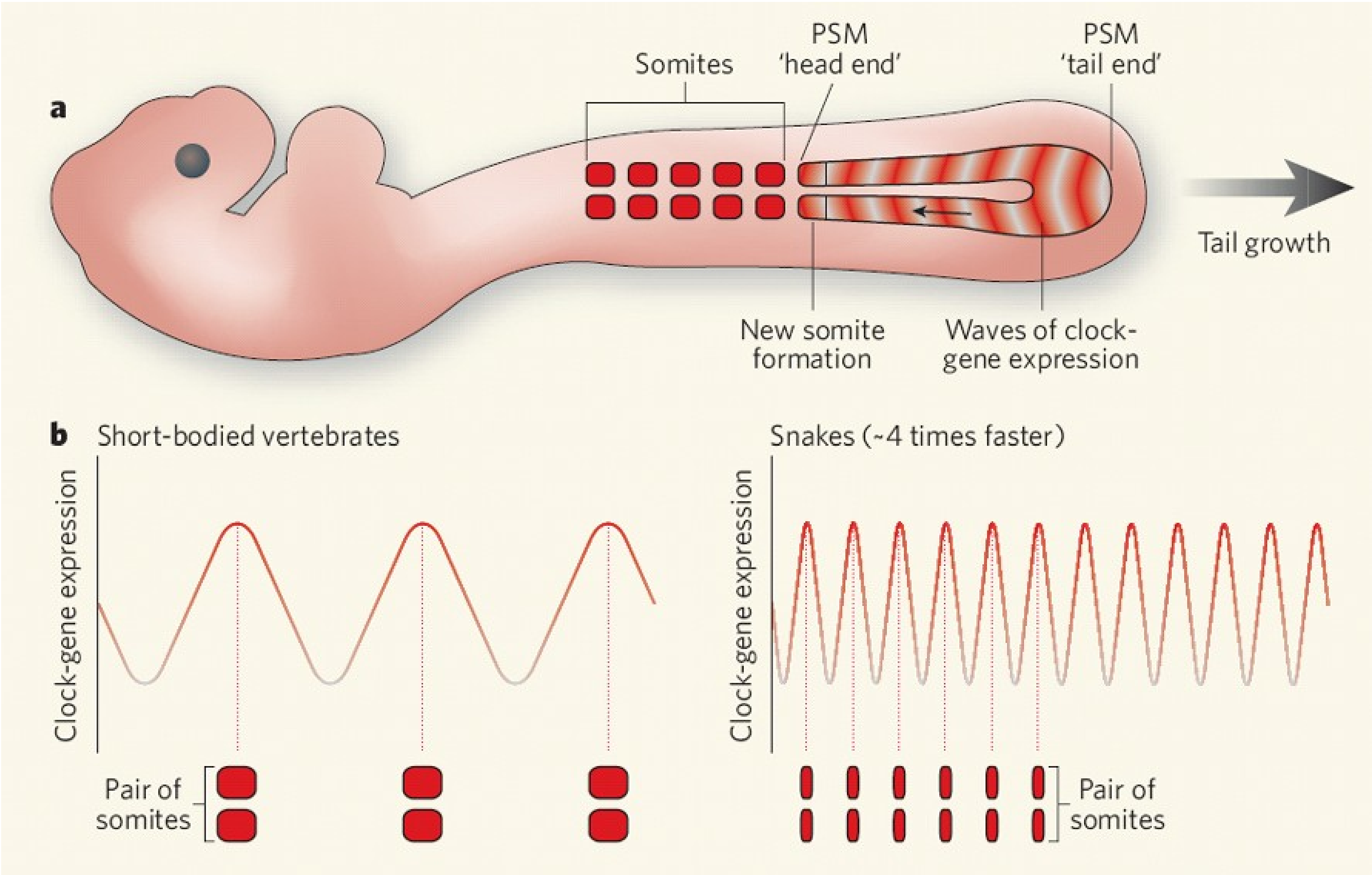
Further Reading:

(1) Friedman N, Vardi S, Ronen M, Alon U, Stavans J (2005) Precise temporal modulation in the response of the SOS DNA repair network in individual bacteria. PloS Biol 3: e238.

(2) Krishna S, Maslov S, Sneppen K (2007) UV-induced mutagenesis in Escherichia coli SOS response: A quantitative model. PLoS Comput Biol 3(3): e41.

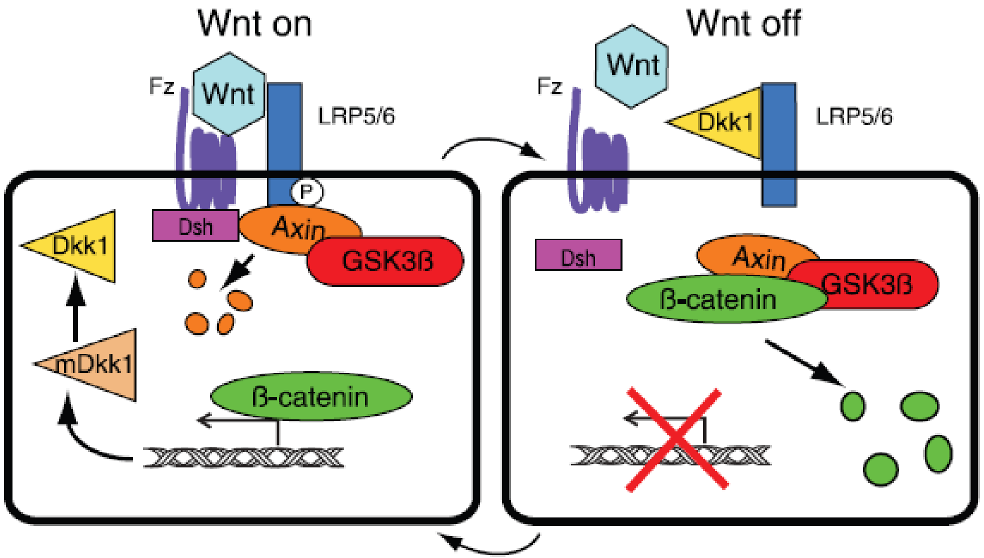
http://2012hs.igem.org/Team:Heidelberg_LSL/Project_SOS

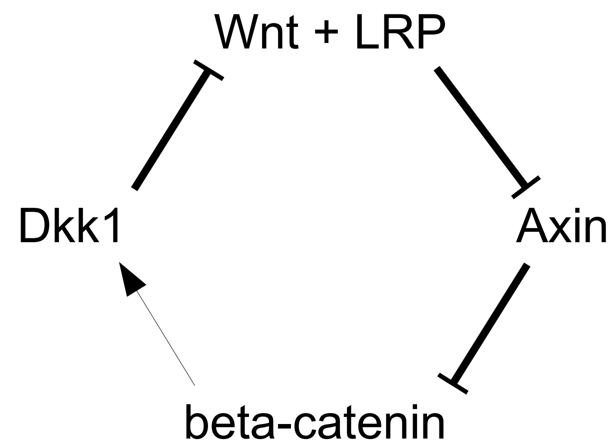
Somitogenesis in vertebrates



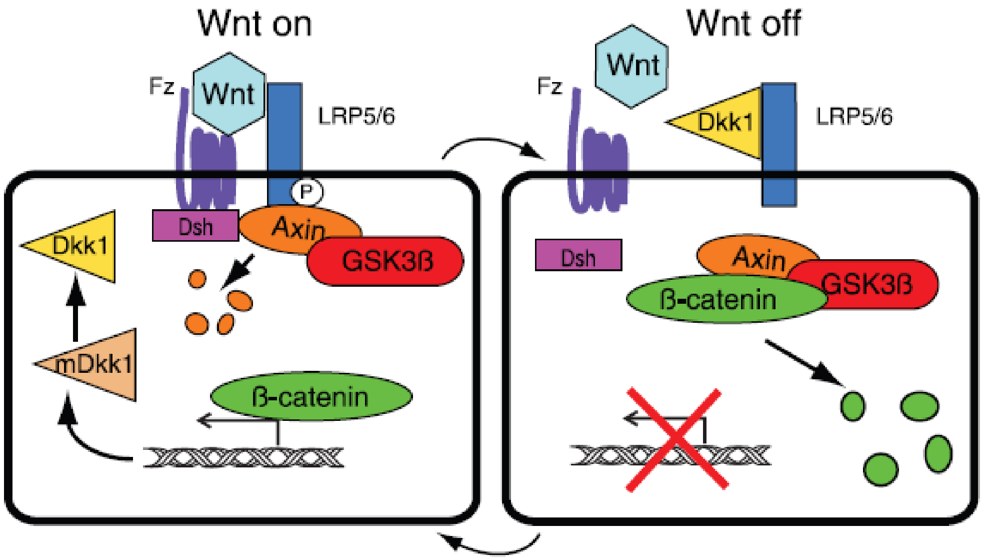
Freek J. Vonk & Michael K. Richardson (2008) Developmental biology: Serpent clocks tick faster. Nature 454, 282-283

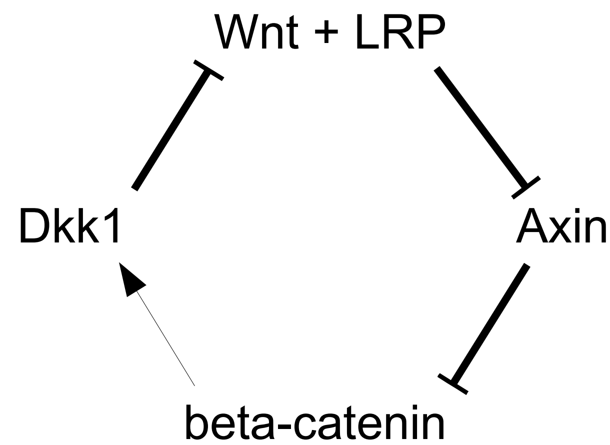
Somitogenesis in vertebrates

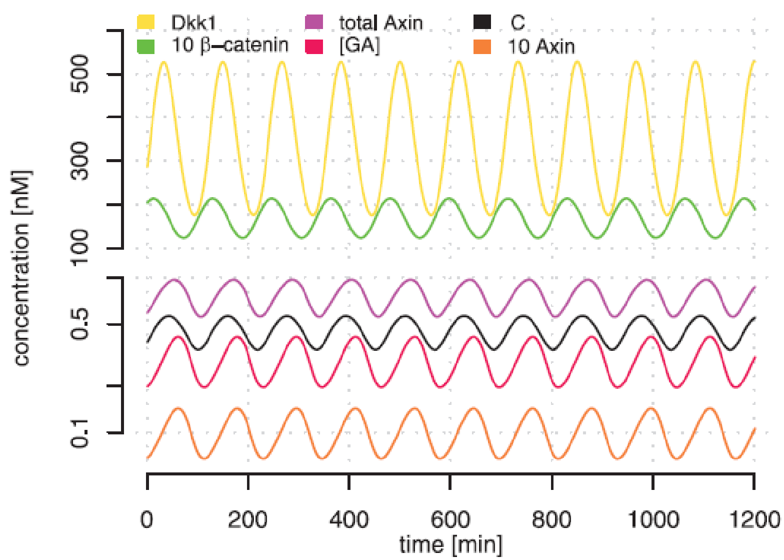




Somitogenesis in vertebrates





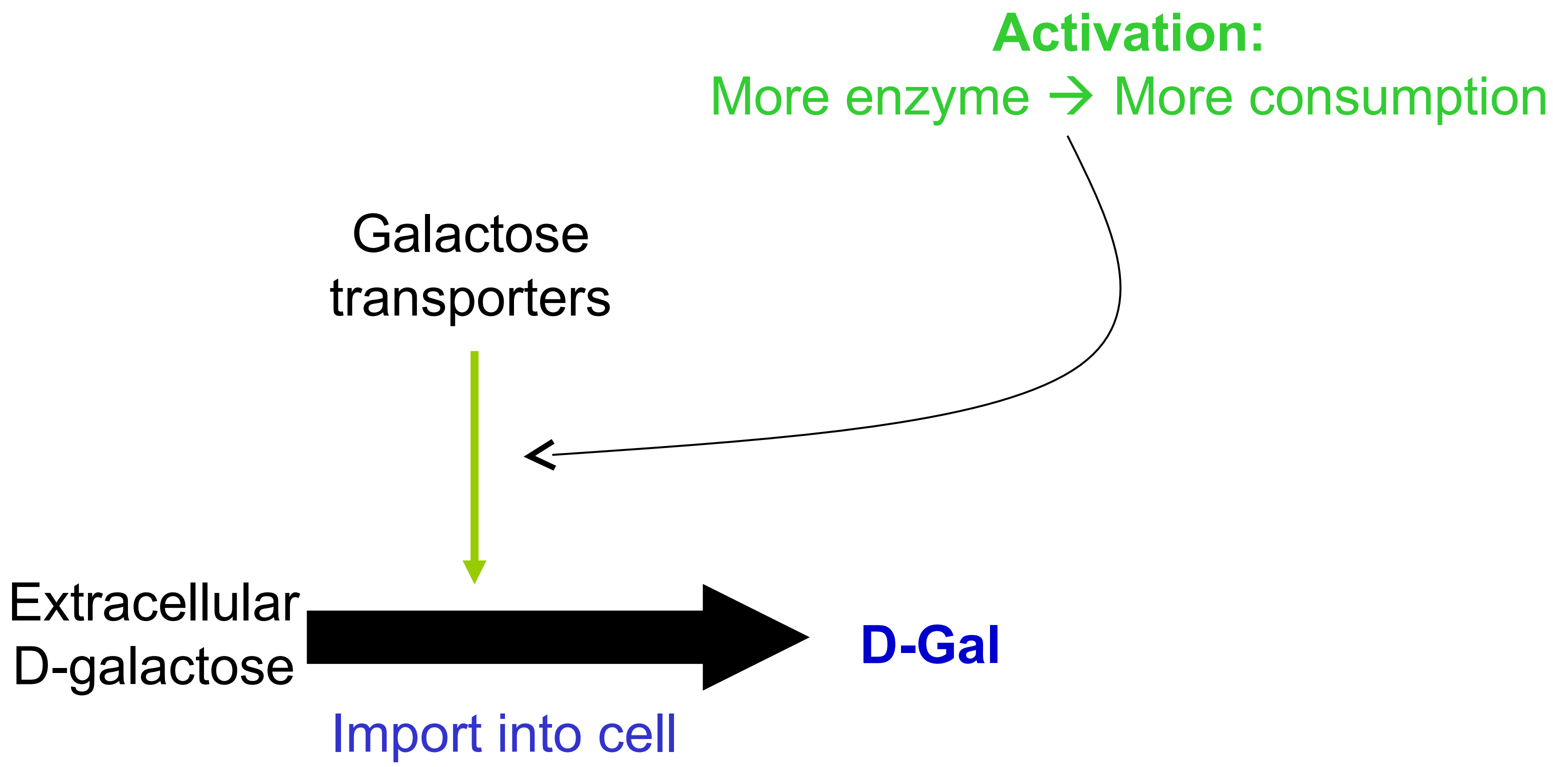


Net result of negative feedback: Oscillations

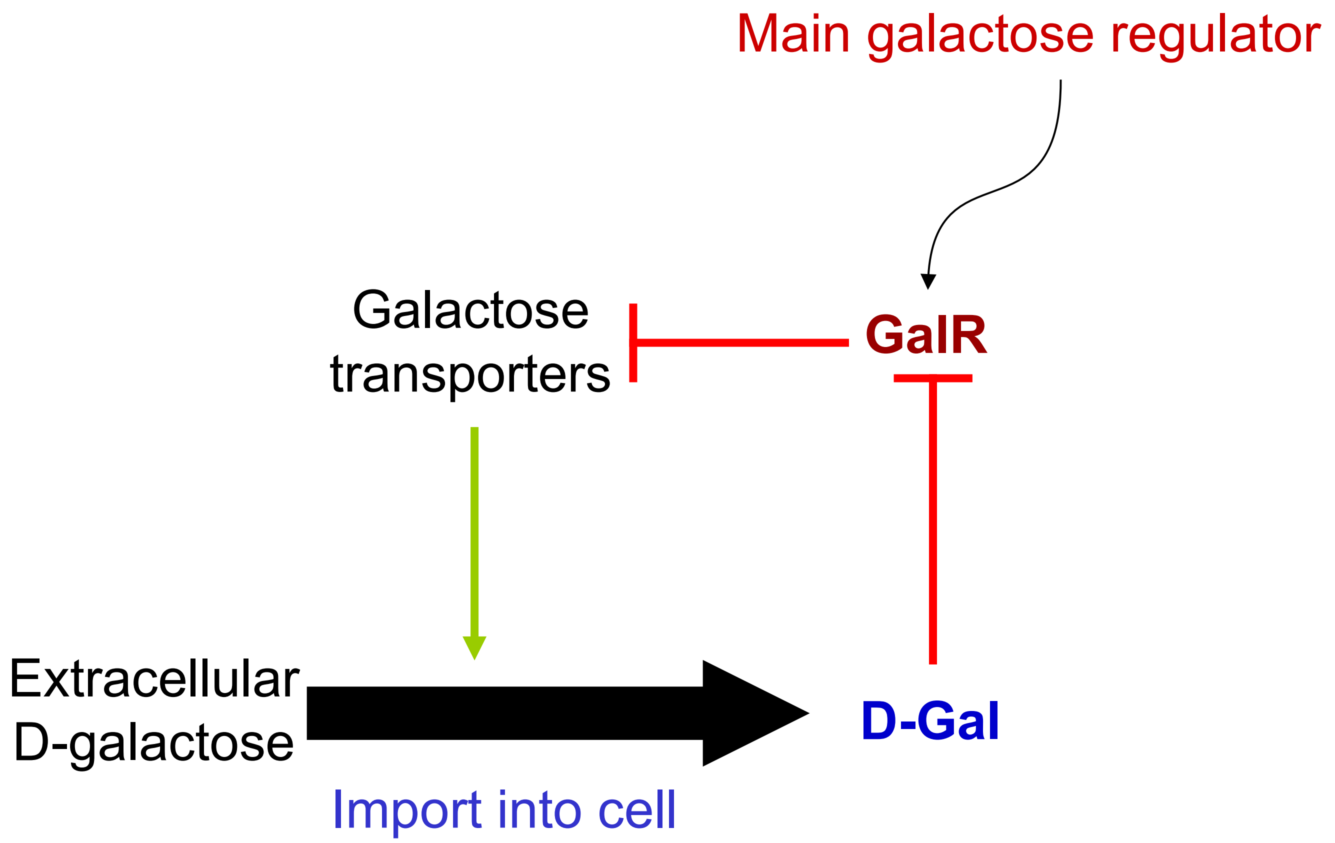
Pedersen L, Jensen MH, Krishna S (2011) Dickkopf1 - A New Player in Modelling the Wnt Pathway. PLoS ONE 6(10): e25550.

Positive Feedback

Galactose network



Galactose network



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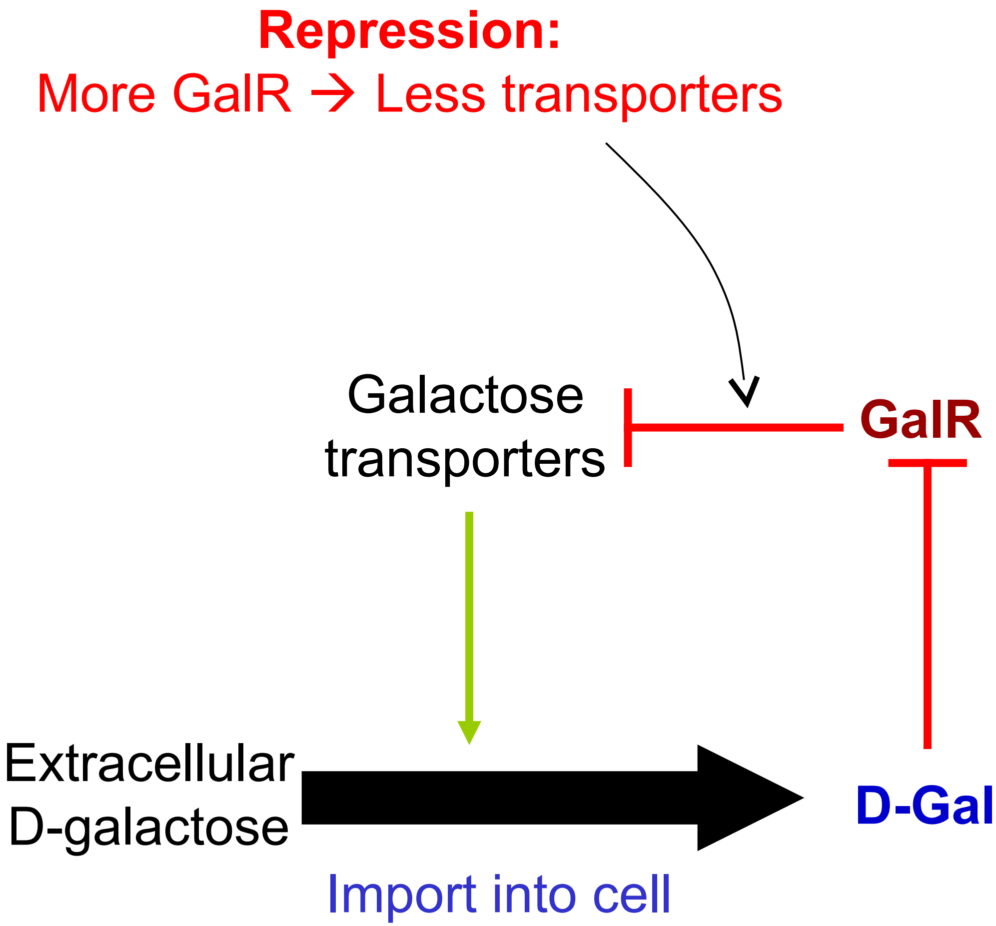

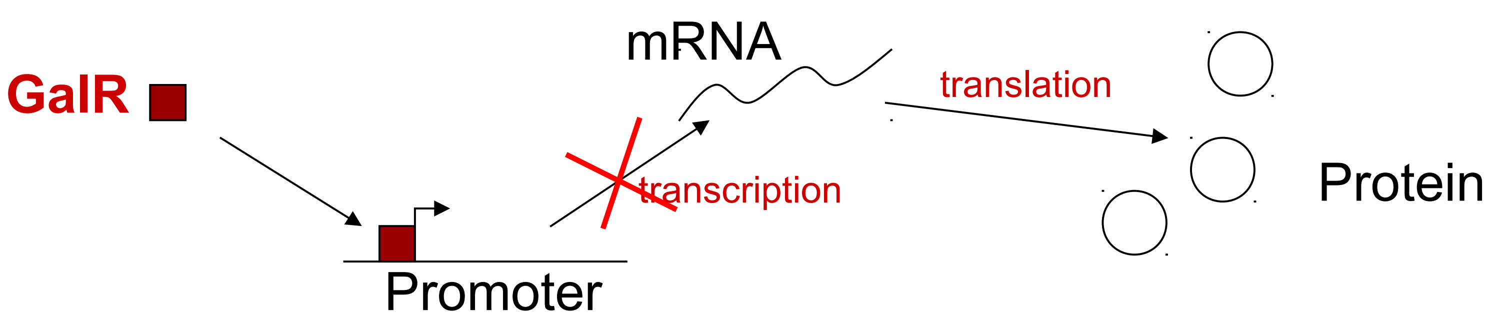

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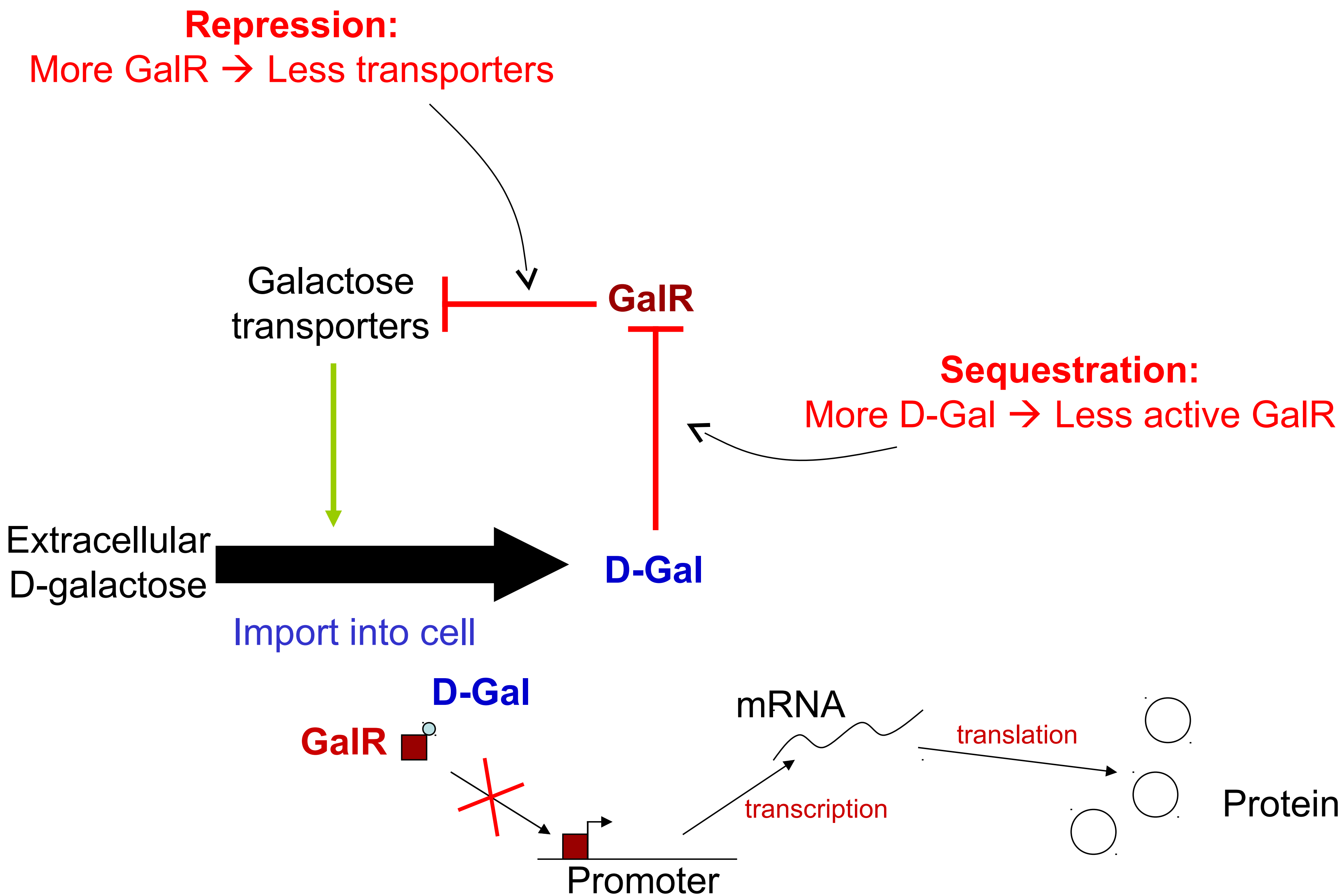

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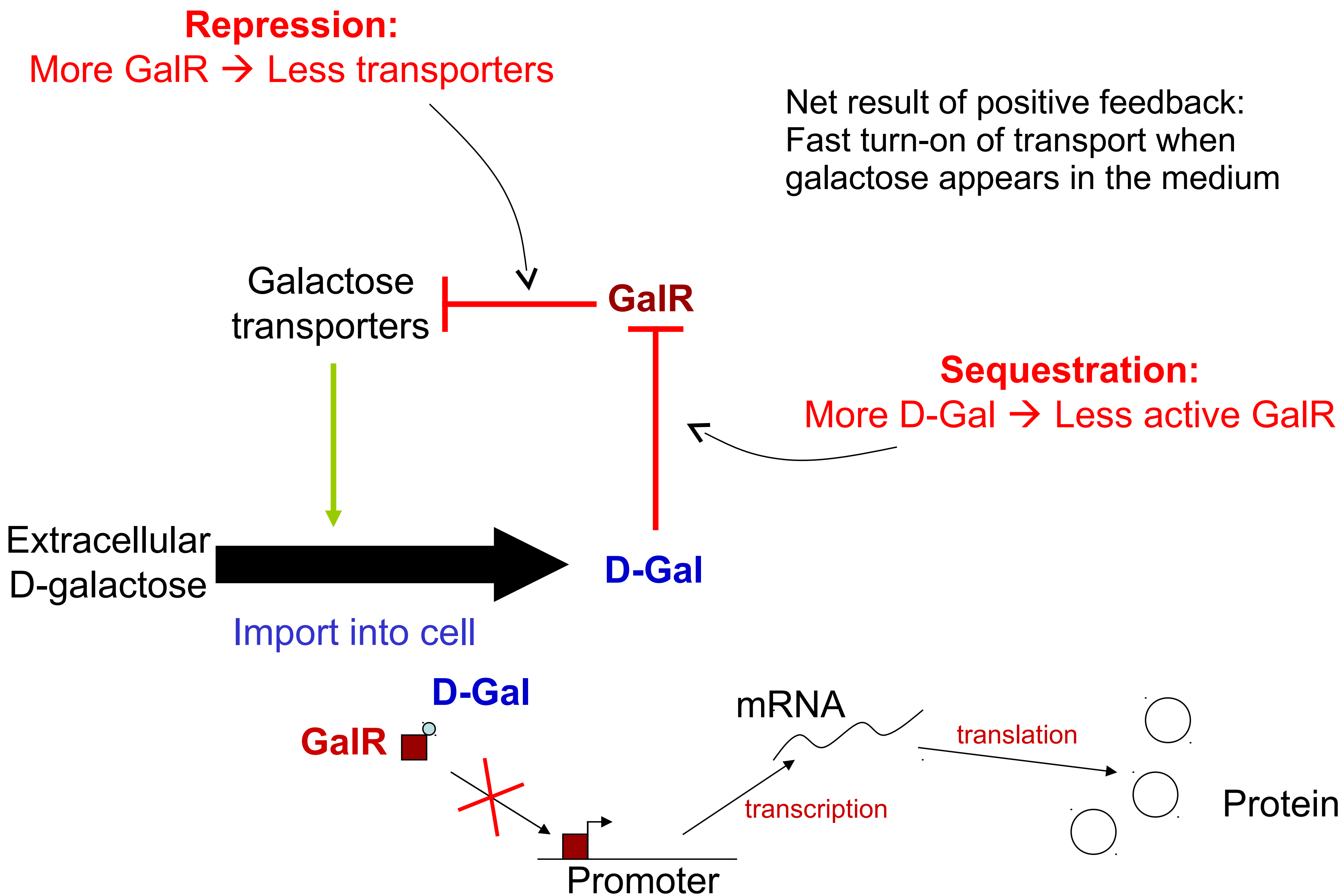
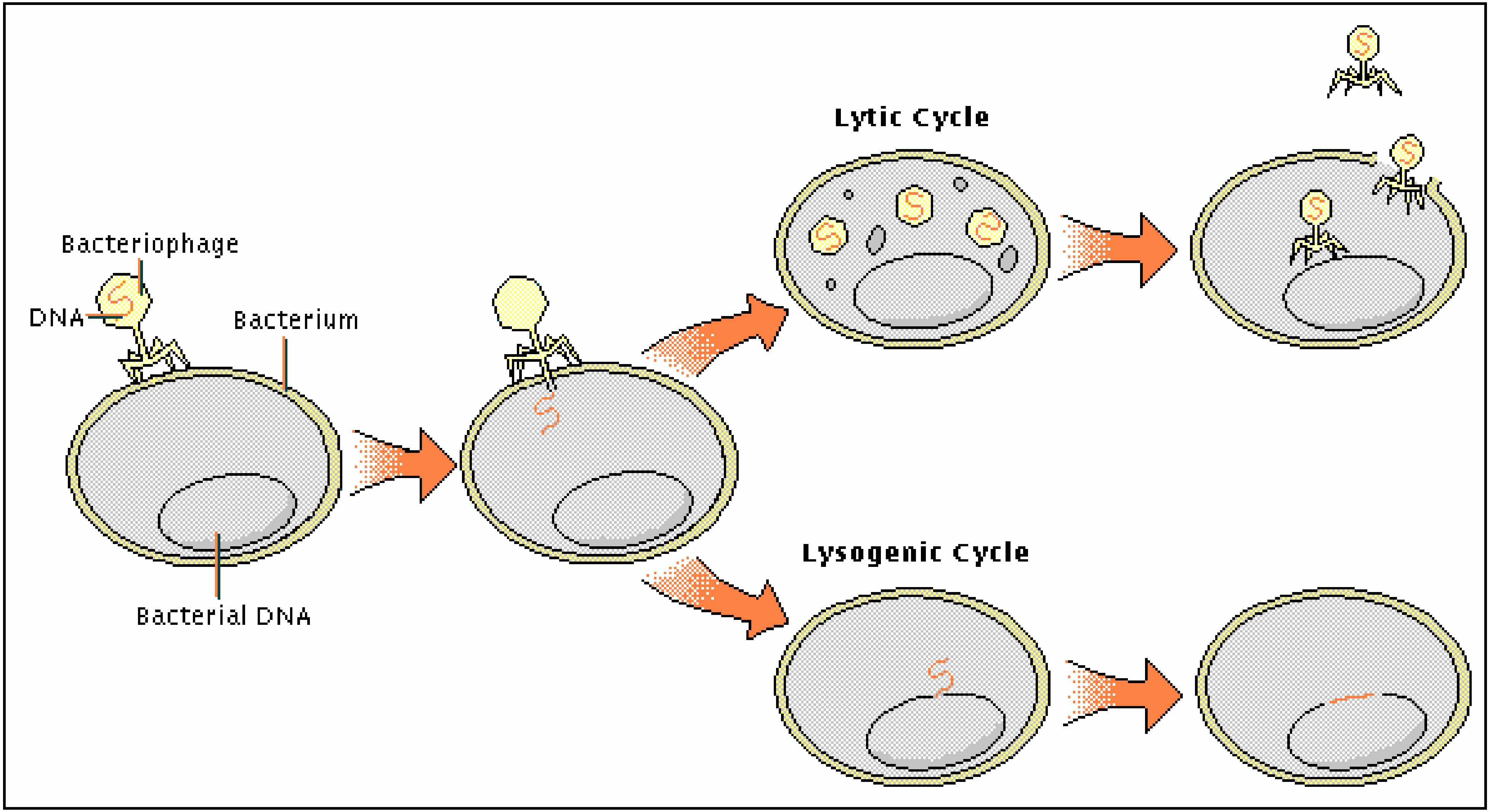
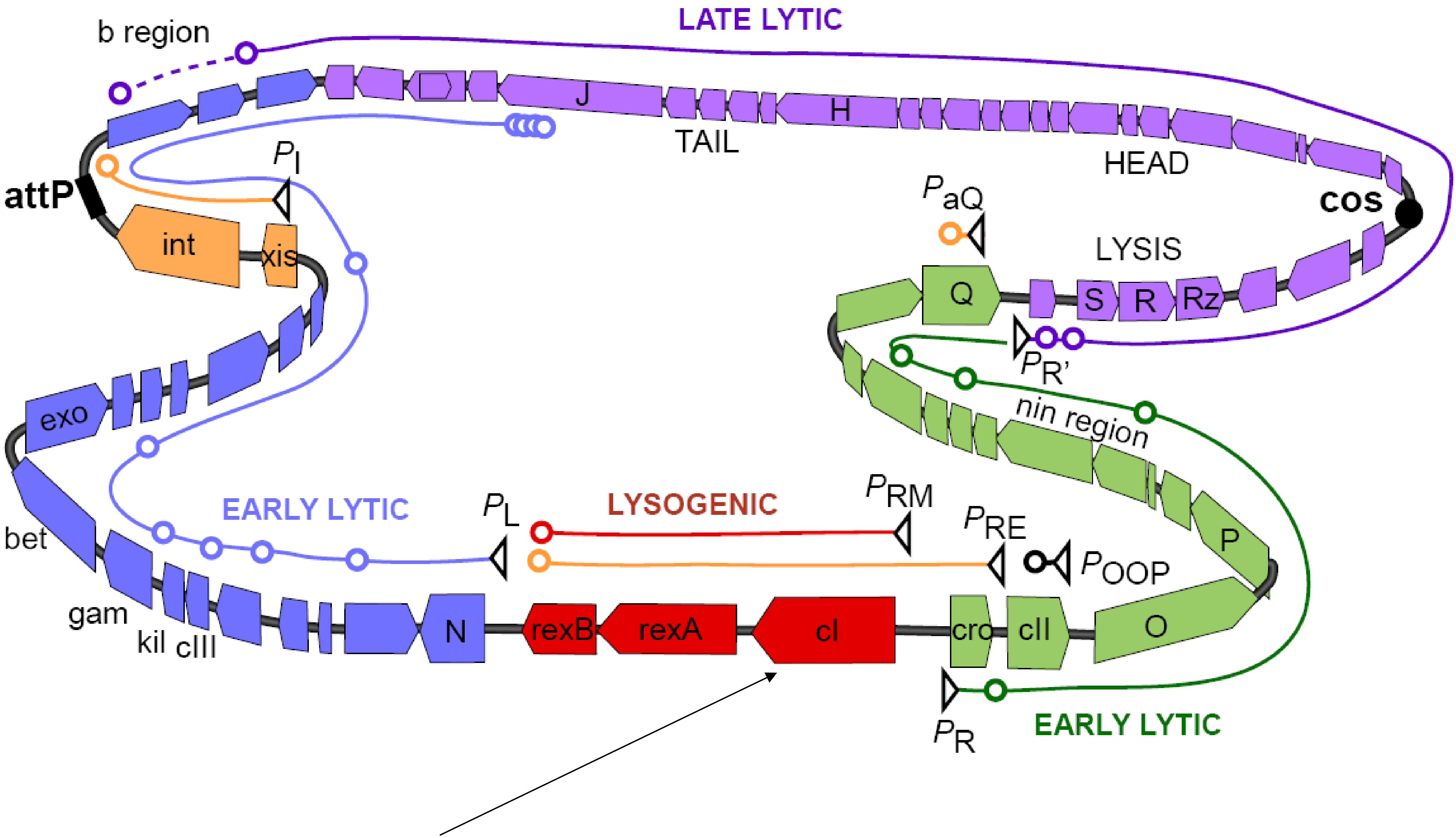


Temperate phage: two different strategies

(example of an underlying bistable system)



Genome of phage λ (which infects E. coli)



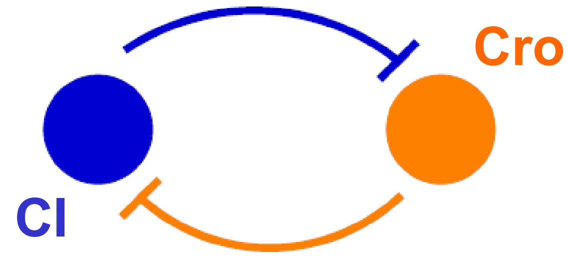
CI: maintains lysogeny, represses all lytic genes

Image courtesy Keith Shearwin, Adelaide Univ.

“Standard model” of λ

Ptashne, A Genetic Switch: Phage Lambda Revisited

Ptashne & Gann, Genes and Signals



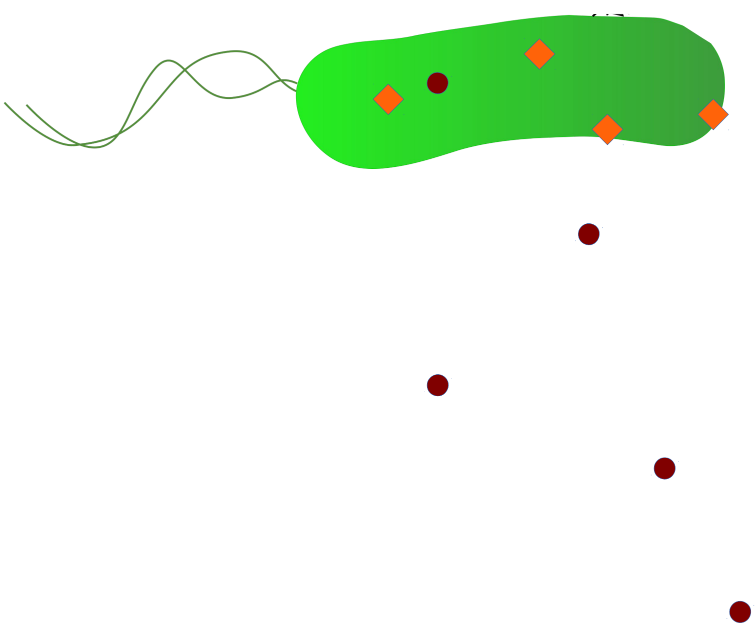
- Simple positive feedback (A represses B; B represses A)
- Net result of positive feedback:

  Two states:

  1. Lytic (CI low, Cro high)
  2. Lysogenic (CI high, Cro low)

Private goods:

- **Ribosomes**
- **Transcription factors**
- etc.



Public goods:

- **Extracellular enzymes** (*P. aeruginosa*: casein proteases)
- **Siderophores** (*P. aeruginosa*: pyoverdine; *E. coli*: enterobactin)

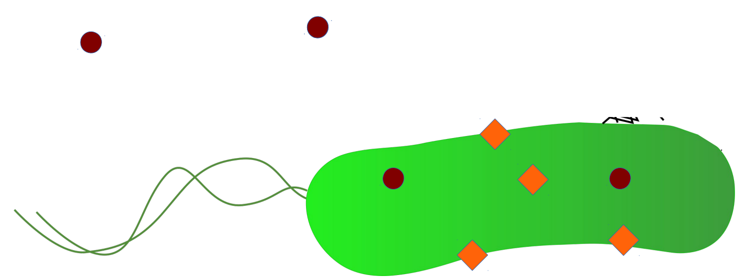
→ Acquiring metabolites

- **Antibacterial compounds** (*P. aeruginosa*: pyocyanin)
- **Virulence factors**

→ Dealing with competition

- **Biofilm** (polysachharides)
- **Surfactants** (rhamnolipids)

→ Changing the environment



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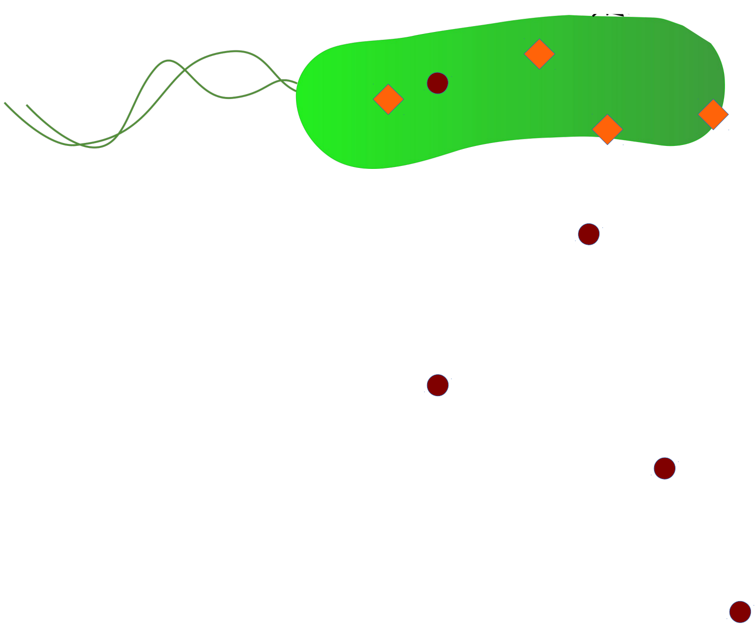

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→ Dealing with competition

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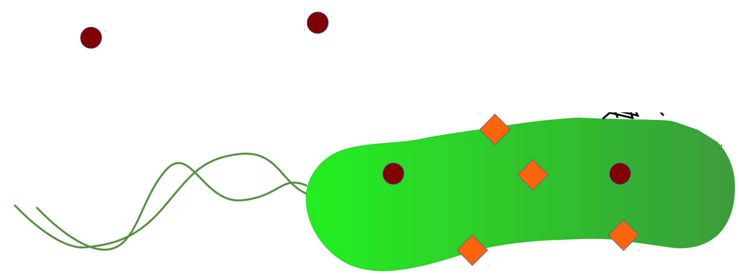
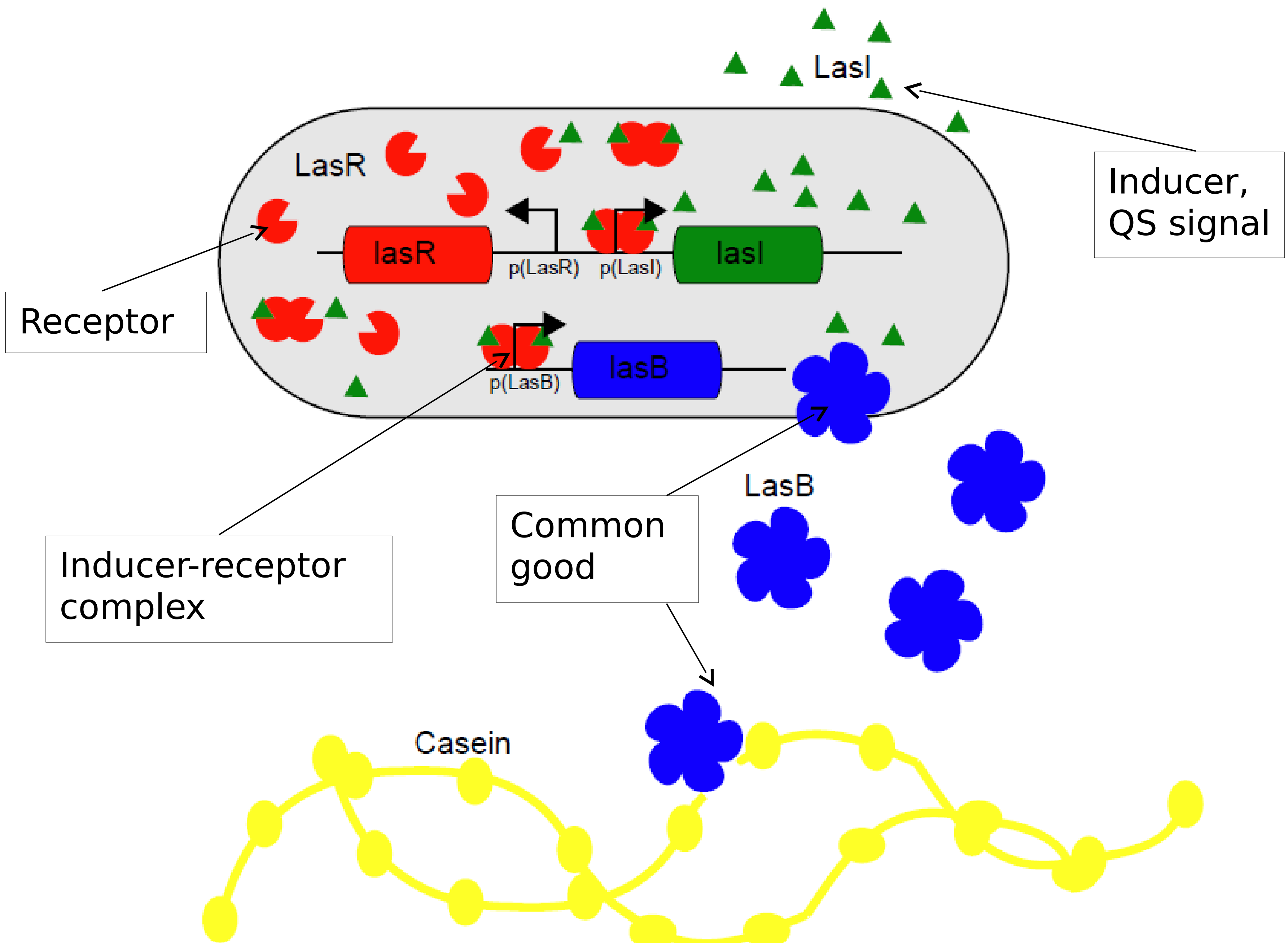
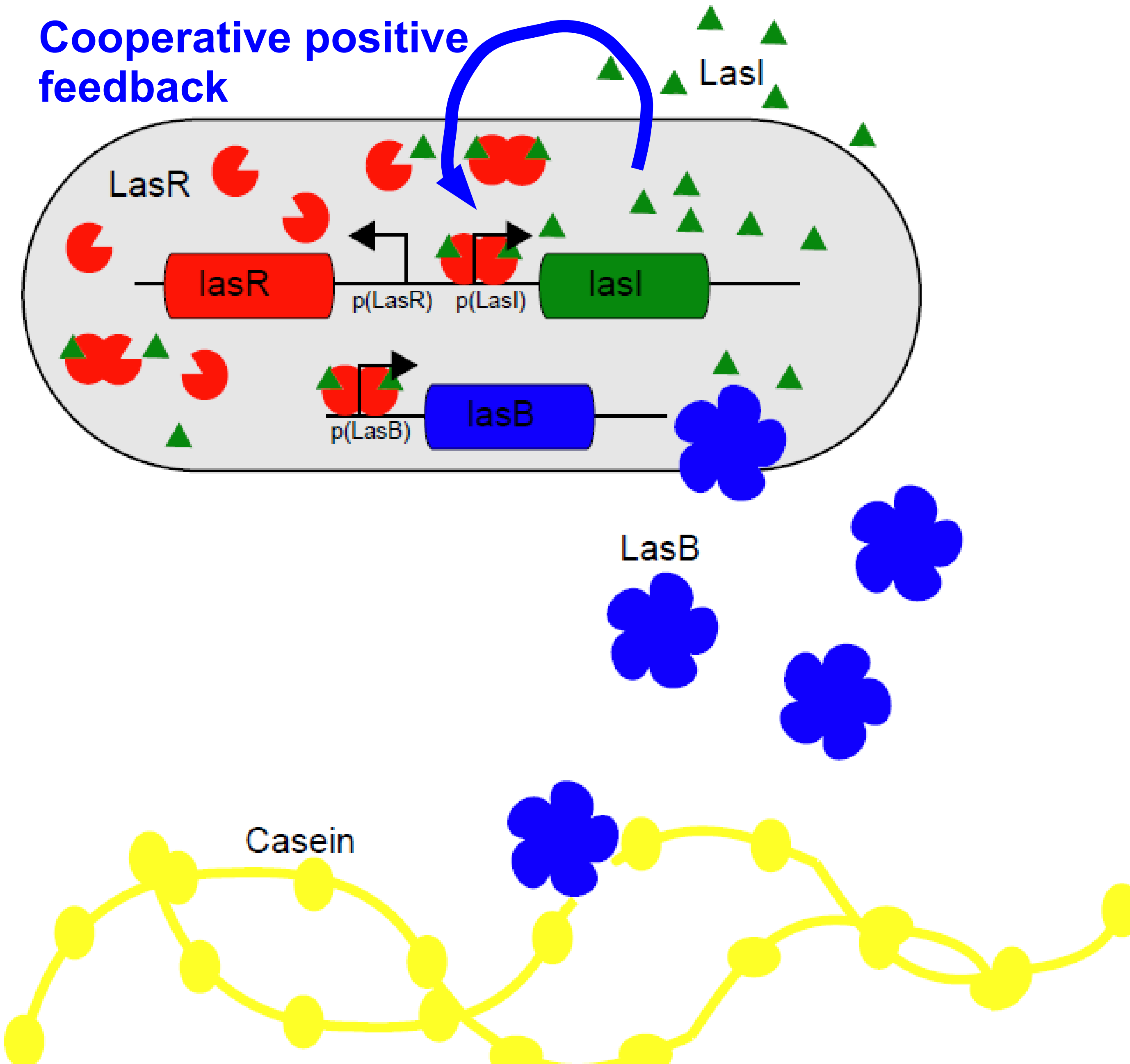


- **Is public good production regulated? (yes!)**
- **When is it beneficial to turn on/off production? (population size)**

Quorum sensing in *P. aeruginosa*



Quorum sensing in *P. aeruginosa*



Negative Feedback

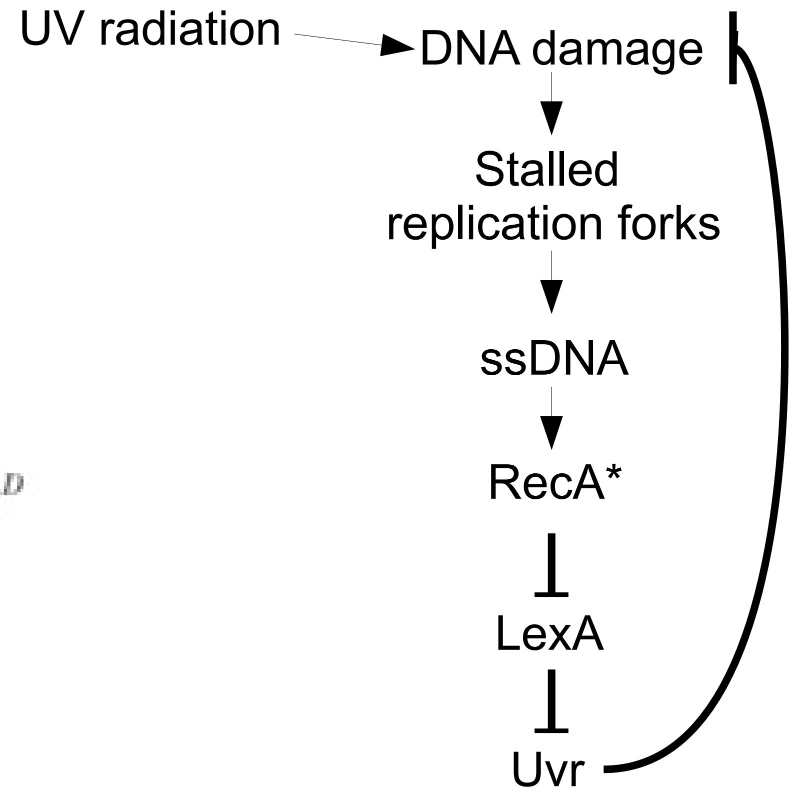
- Homeostasis
- Pulse-like dynamics
- Oscillations
- Reducing noise

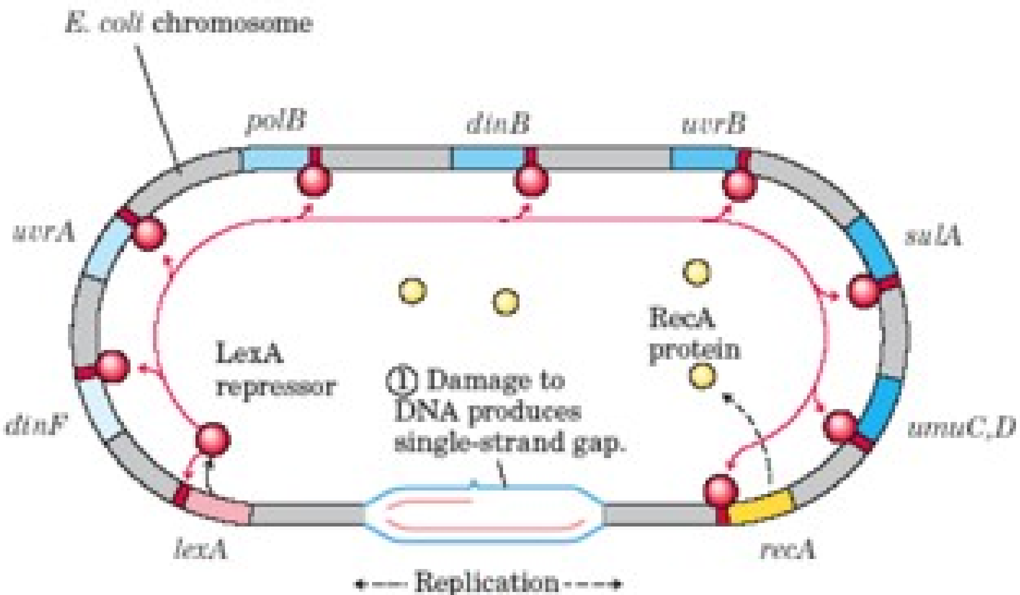
Positive Feedback

- Fast turn-on (switch like behaviour)
- Multiple states (bi- or multi-stability)
- Synchronizing a population
- Amplifying noise

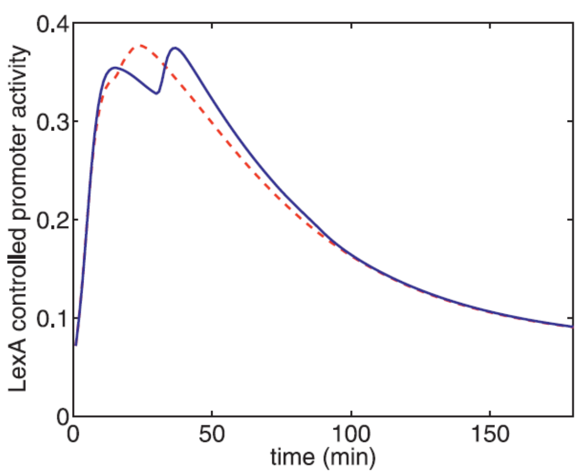
Life is always more complicated

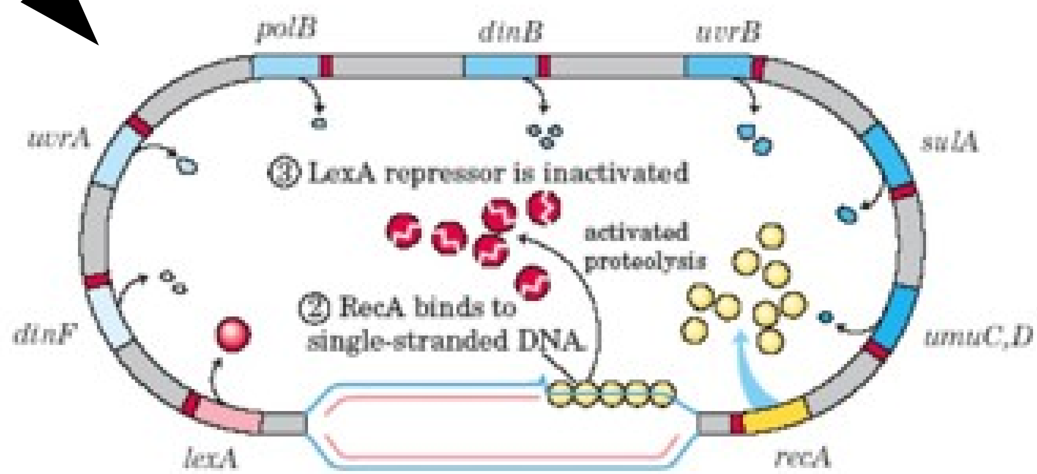
SOS response to DNA damage in E. coli





Net result of negative feedback: Homeostasis





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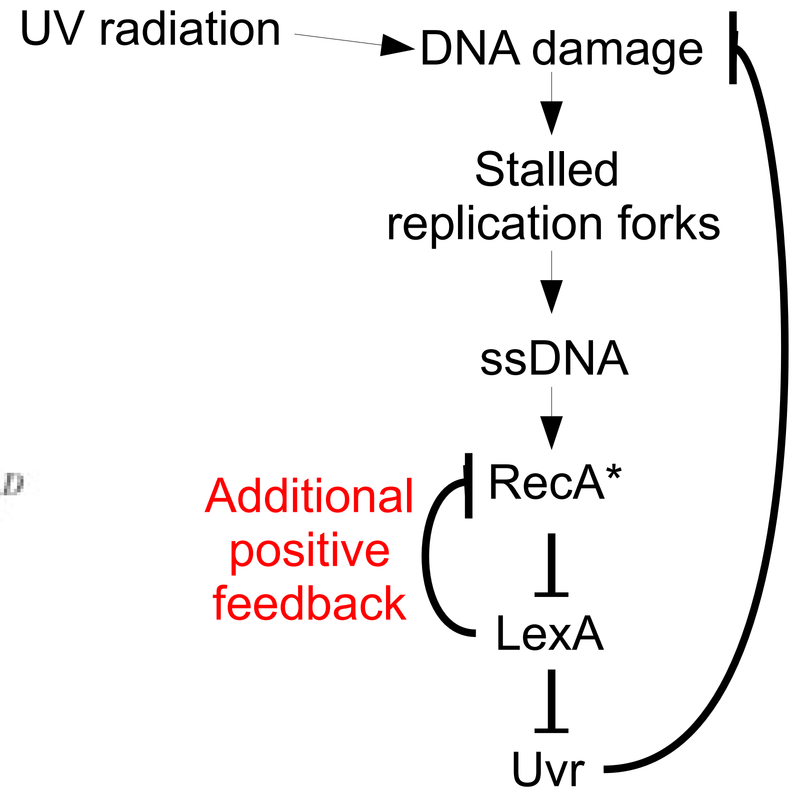

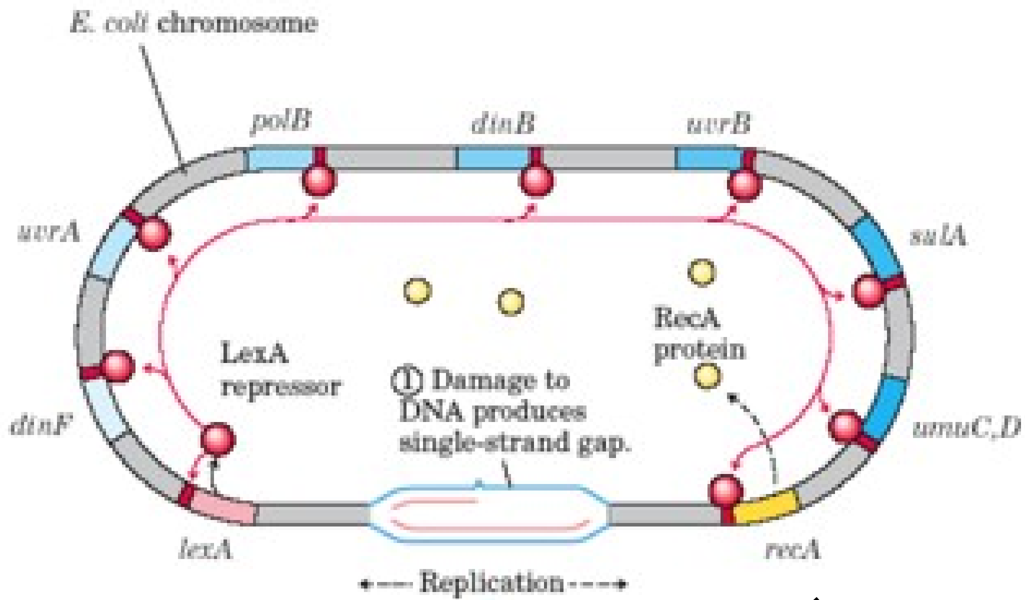

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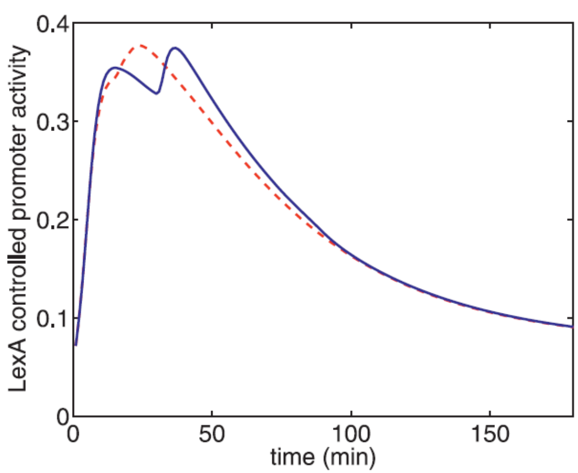

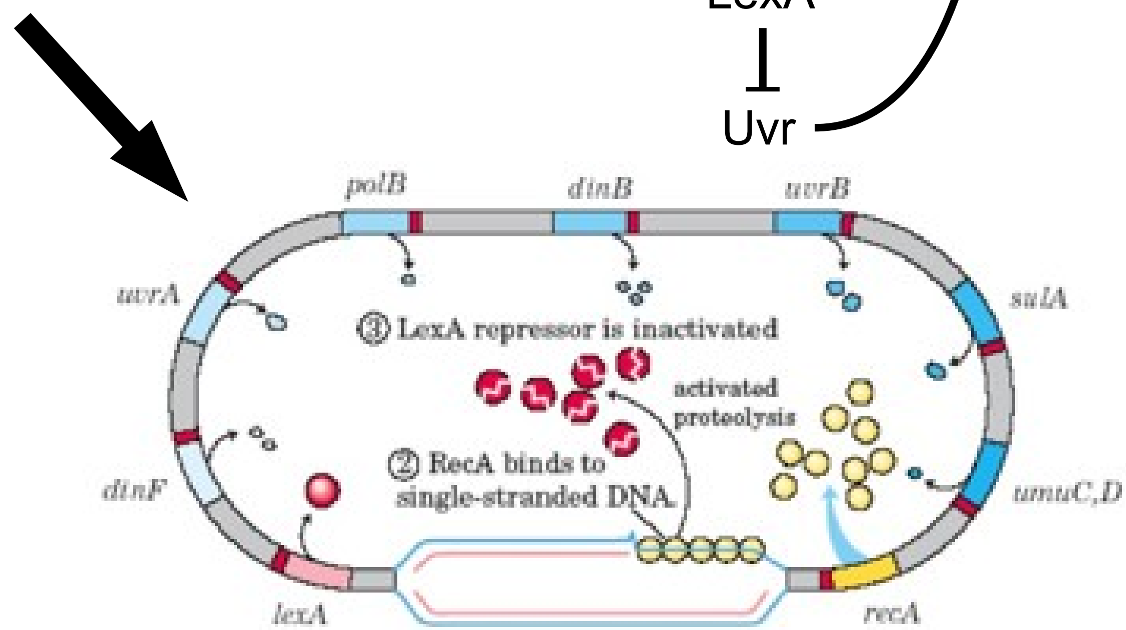

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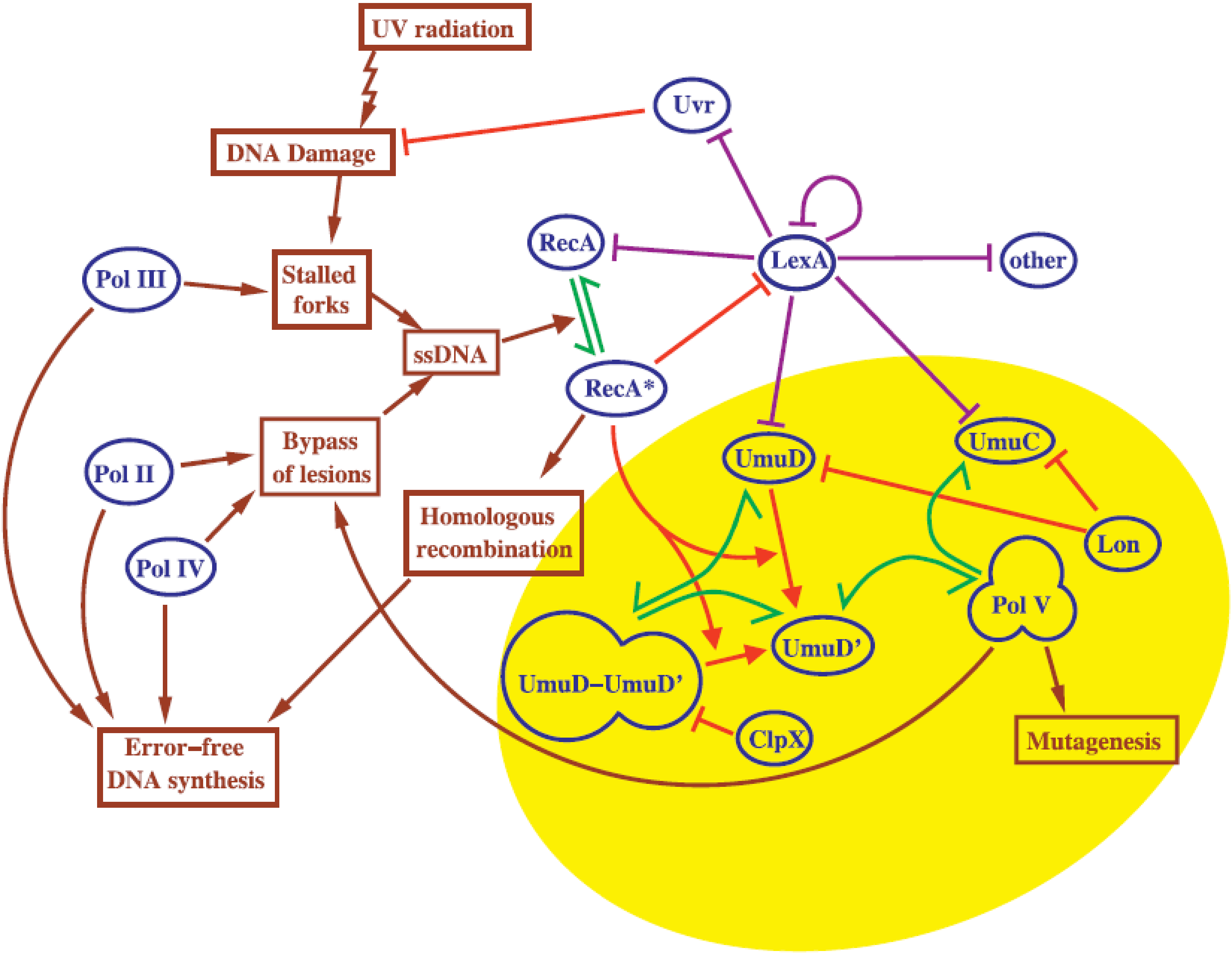
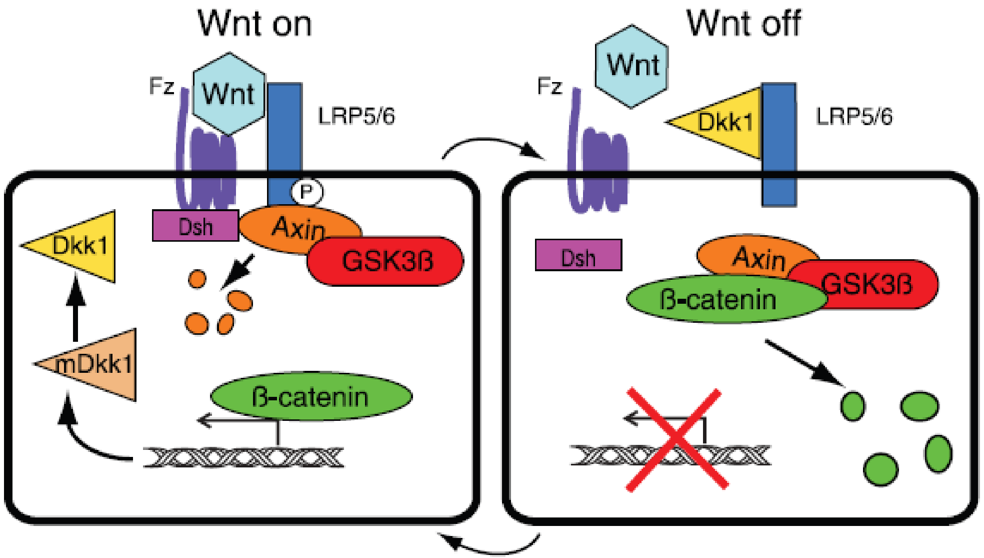
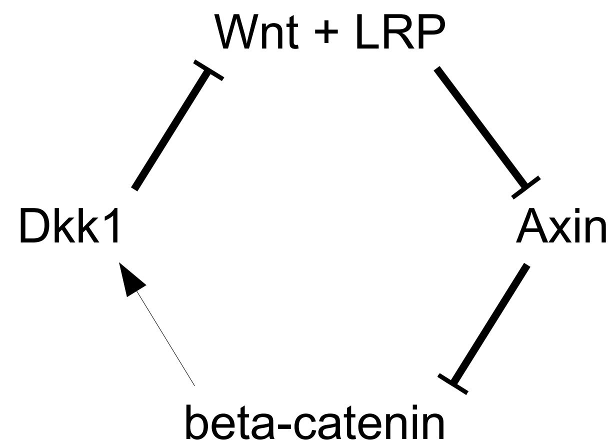
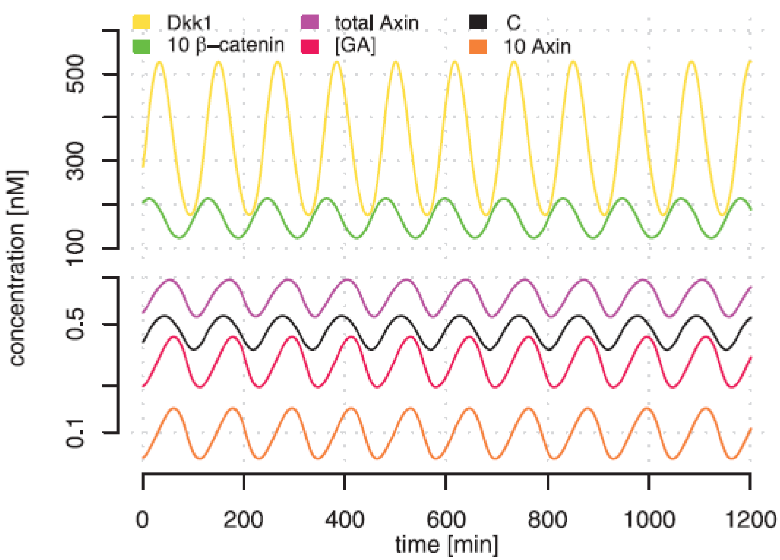


Krishna S, Maslov S, Sneppen K (2007) UV-induced mutagenesis in Escherichia coli SOS response: A quantitative model. PLoS Comput Biol 3(3): e41.

Somitogenesis in vertebrates



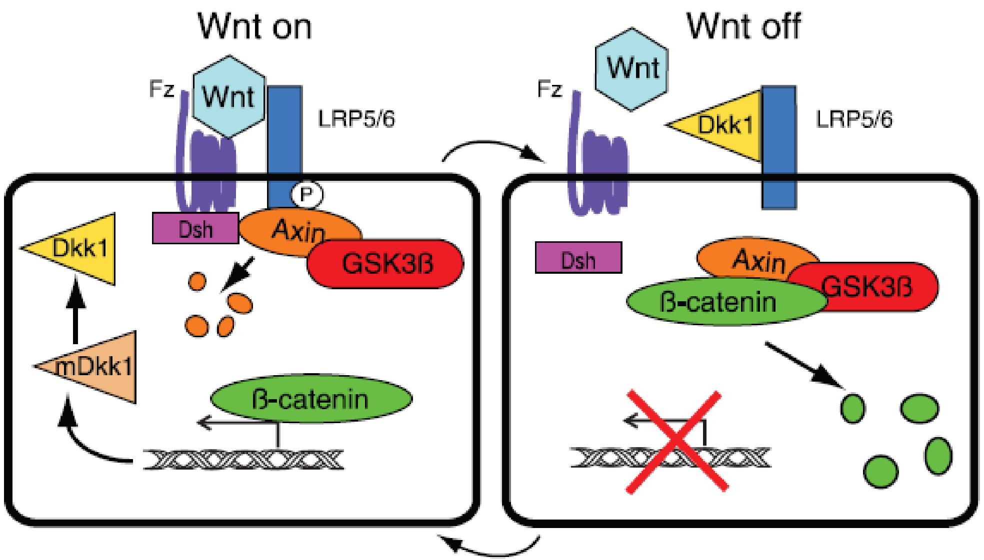




Net result of negative feedback: Oscillations

Pedersen L, Jensen MH, Krishna S (2011) Dickkopf1 - A New Player in Modelling the Wnt Pathway. PLoS ONE 6(10): e25550.

Somitogenesis in vertebrates



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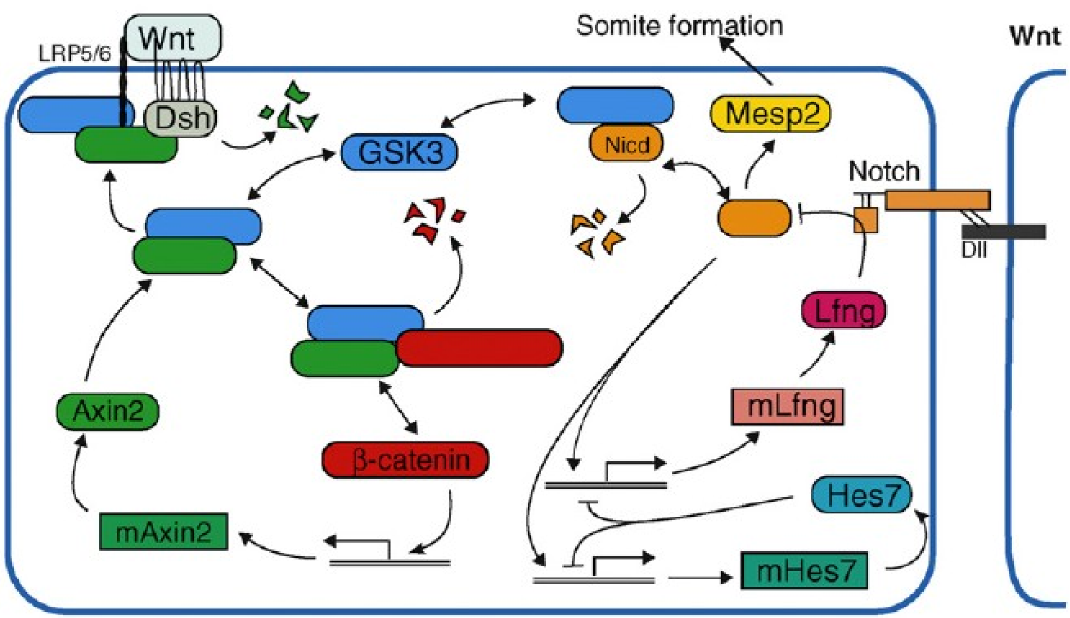
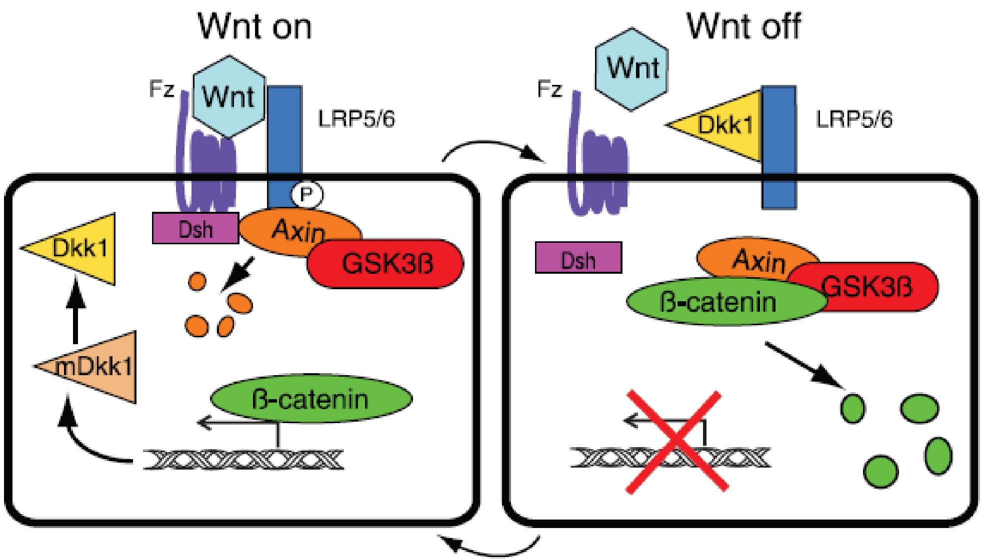
New feedback loops keep being discovered (although they all seem to be negative feedback)



Mengel, et al. Modeling oscillatory control in NF-kB, p53 and Wnt signaling, Curr. Opin. Genet. Dev. (2010)

Somitogenesis in vertebrates



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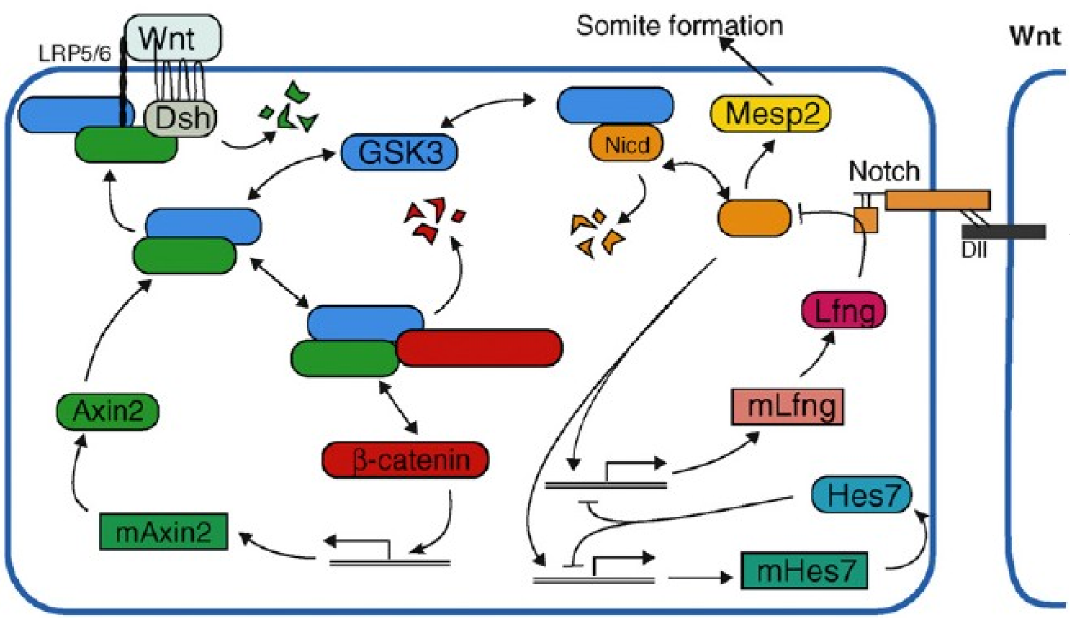
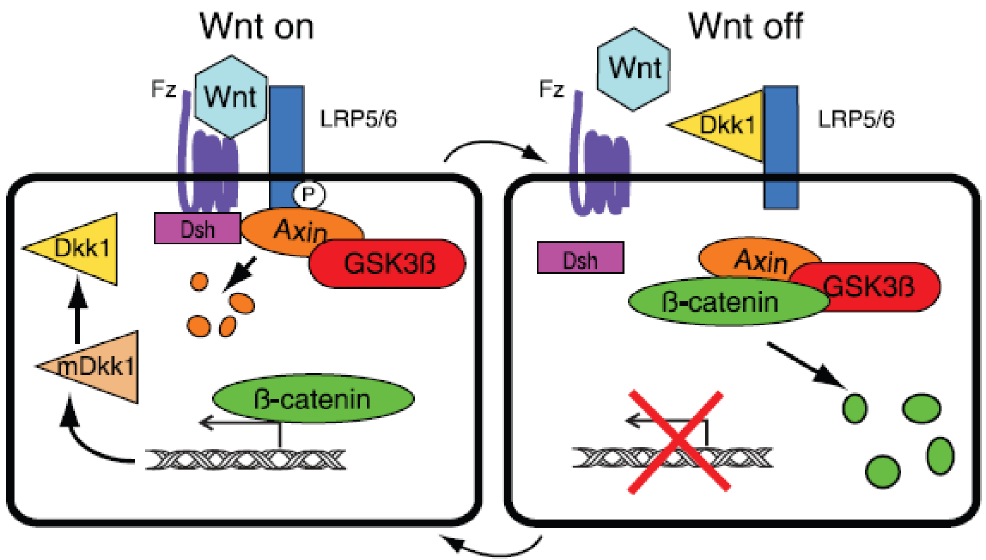


New feedback loops keep being discovered (although they all seem to be negative feedback)

Except for the cell-cell interaction which seems to be a positive feedback loop

Mengel, et al. Modeling oscillatory control in NF-kB, p53 and Wnt signaling, Curr. Opin. Genet. Dev. (2010)

Somitogenesis in vertebrates



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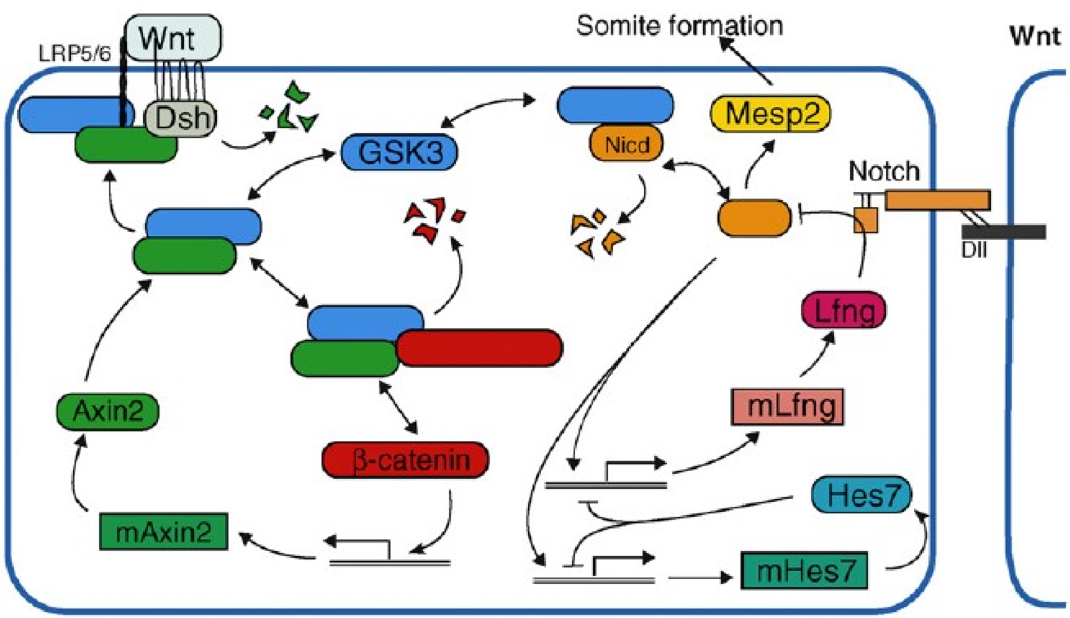


Mengel, et al. Modeling oscillatory control in NF-kB, p53 and Wnt signaling, Curr. Opin. Genet. Dev. (2010)

Further Reading:

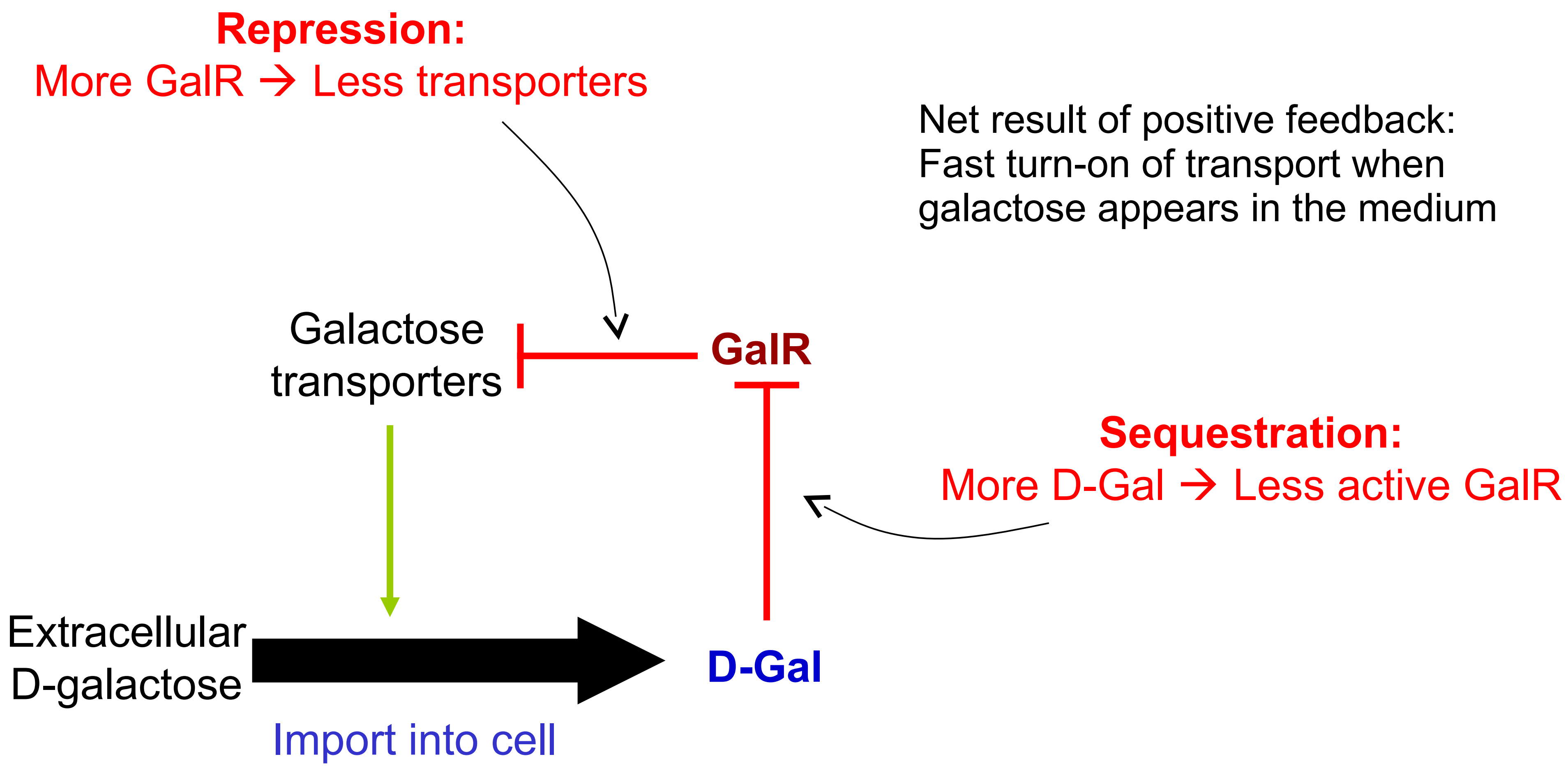
Dequeant ML, et al.(2006) A complex oscillating network of signaling genes underlies the mouse segmentation clock. Science 314:1595-1598.

Aulehla A, et al. (2008) A beta-catenin gradient links the clock and wave front systems in mouse embryo segmentation. Nat Cell Biol 10:168-210.

Jensen PB, Pedersen L, Krishna S, Jensen MH (2010) A wnt oscillator model for somitogenesis. Biophys J 98: 943–50.

How to convert an oscillation in time into a periodic spatial pattern for somites:
Cooke J, Zeeman EC (1976) A clock and wavefront model for control of the number of repeated structures during animal morphogenesis.
J Theor Biol 58: 455–476.

Galactose network



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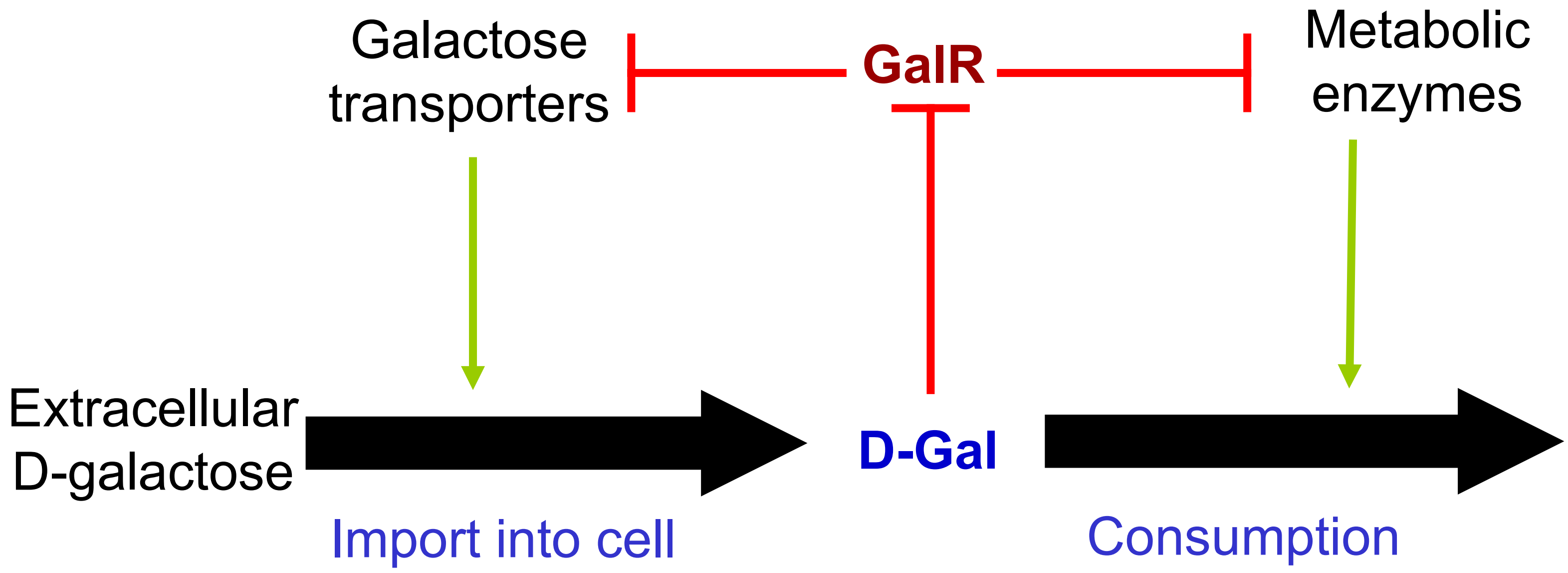

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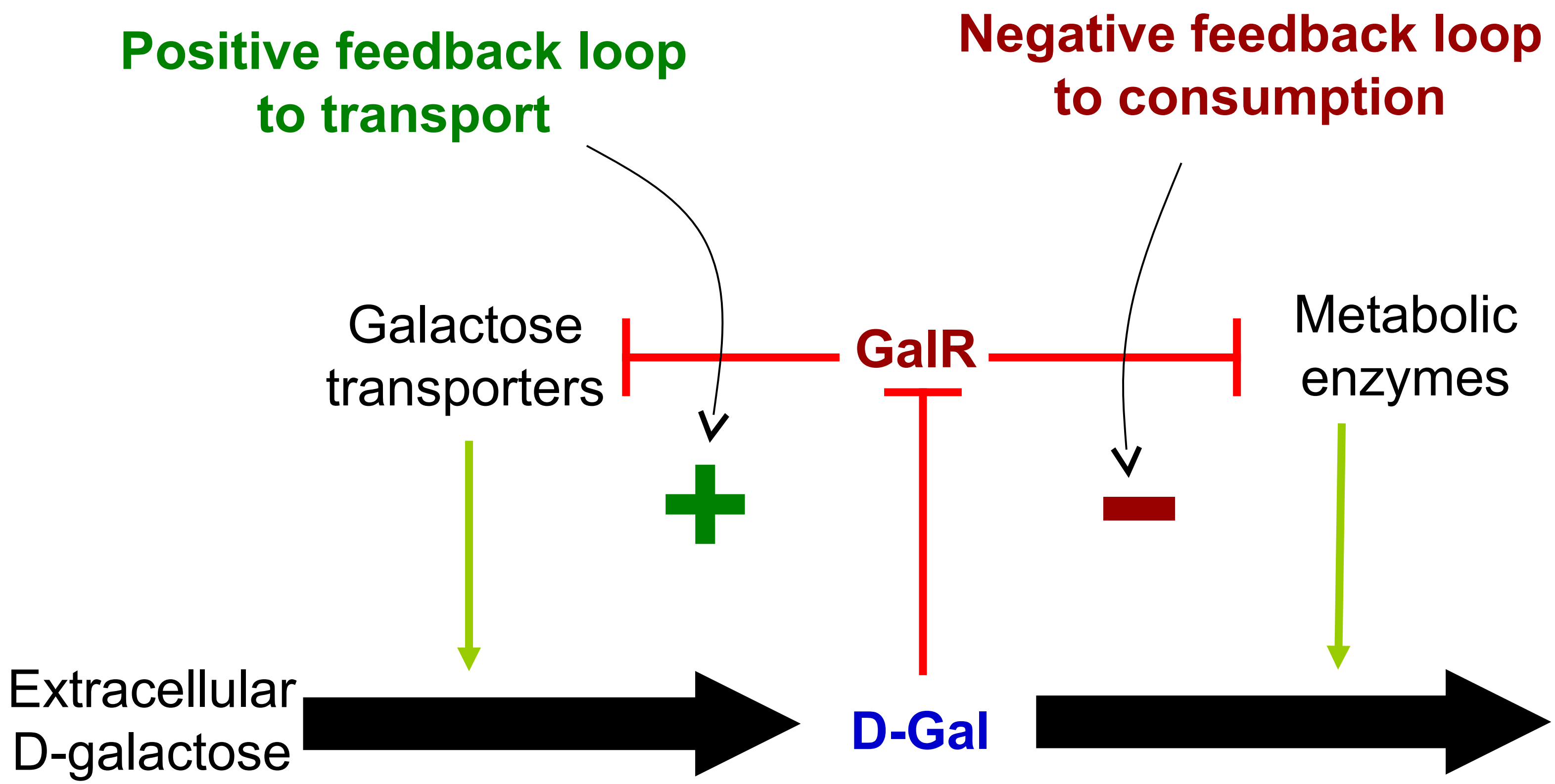
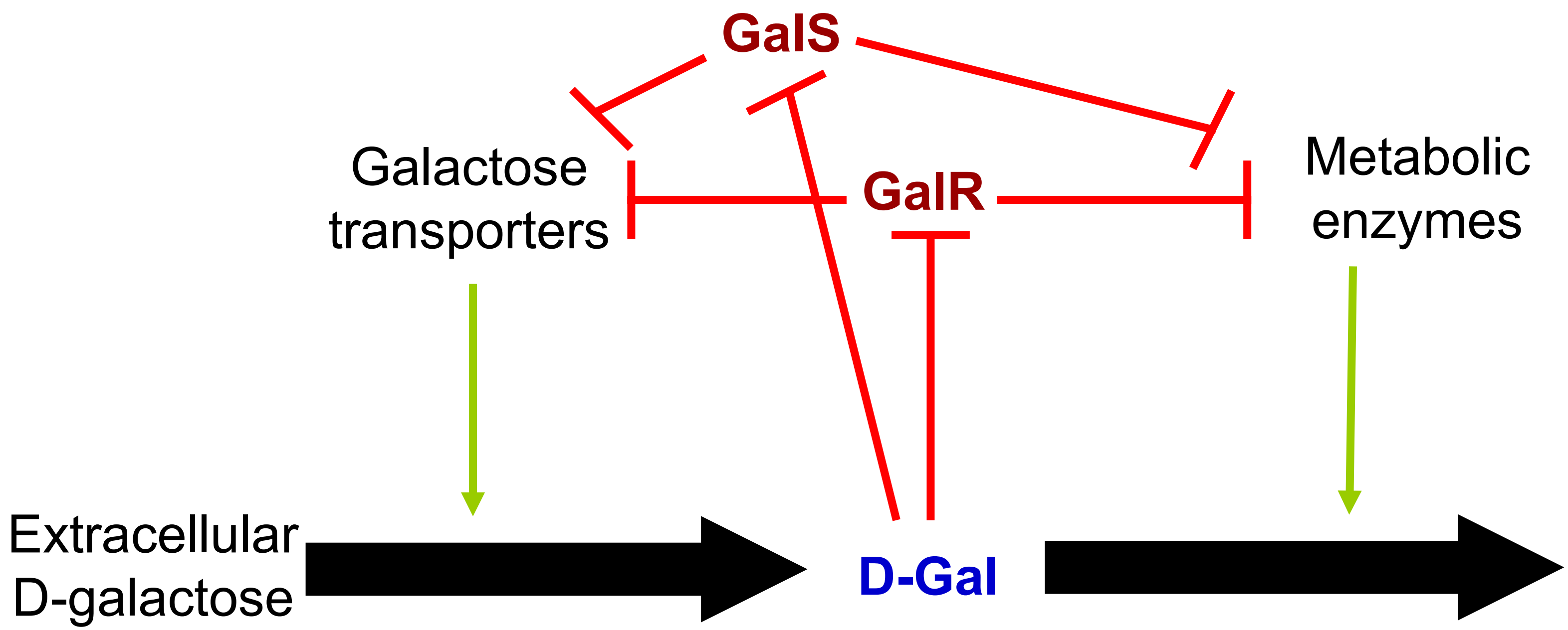


When D-gal is detected, both transport and consumption are increased

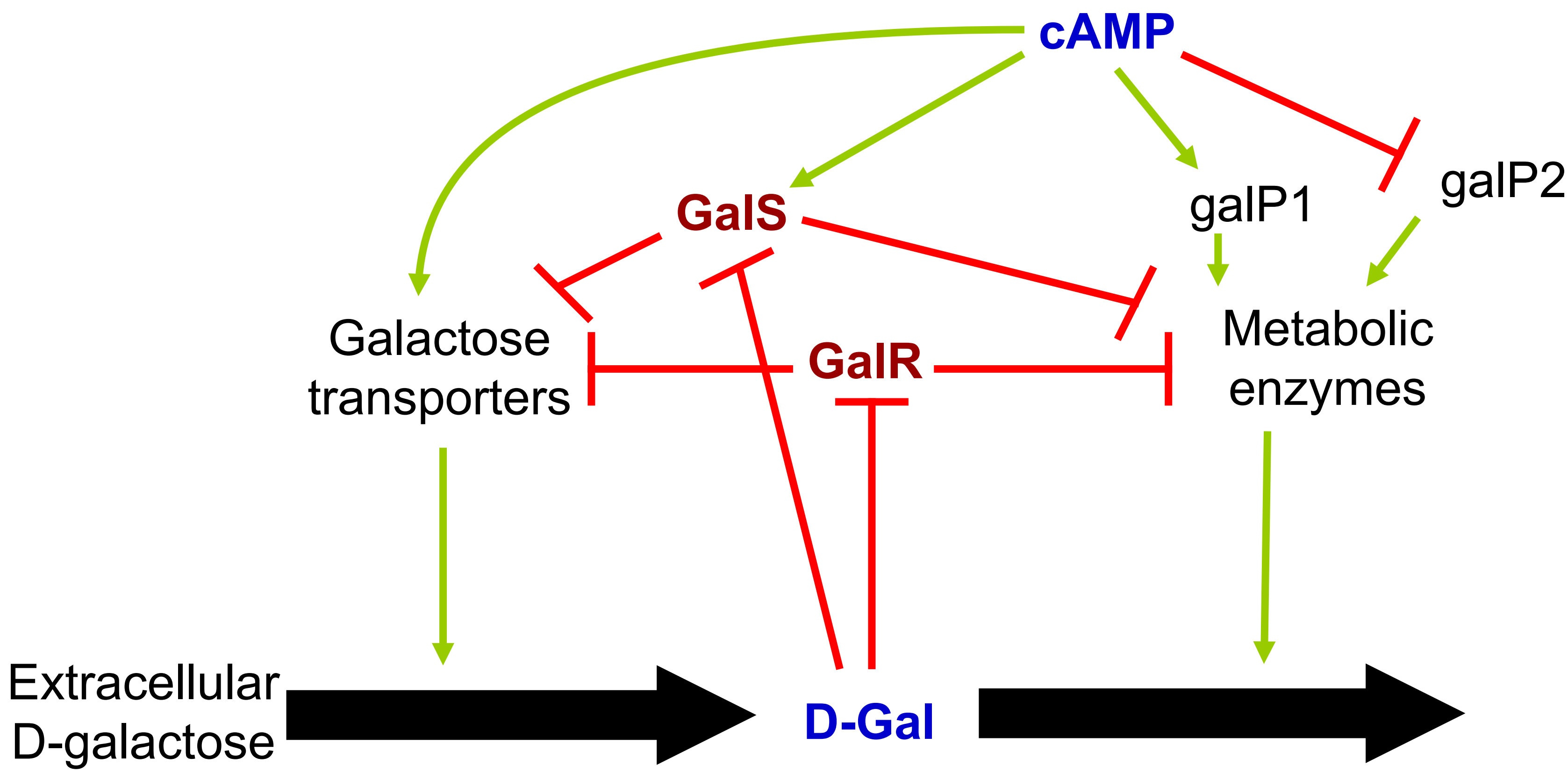
This (+ -) two-loop feedback motif maximizes flow through the system

Galactose network



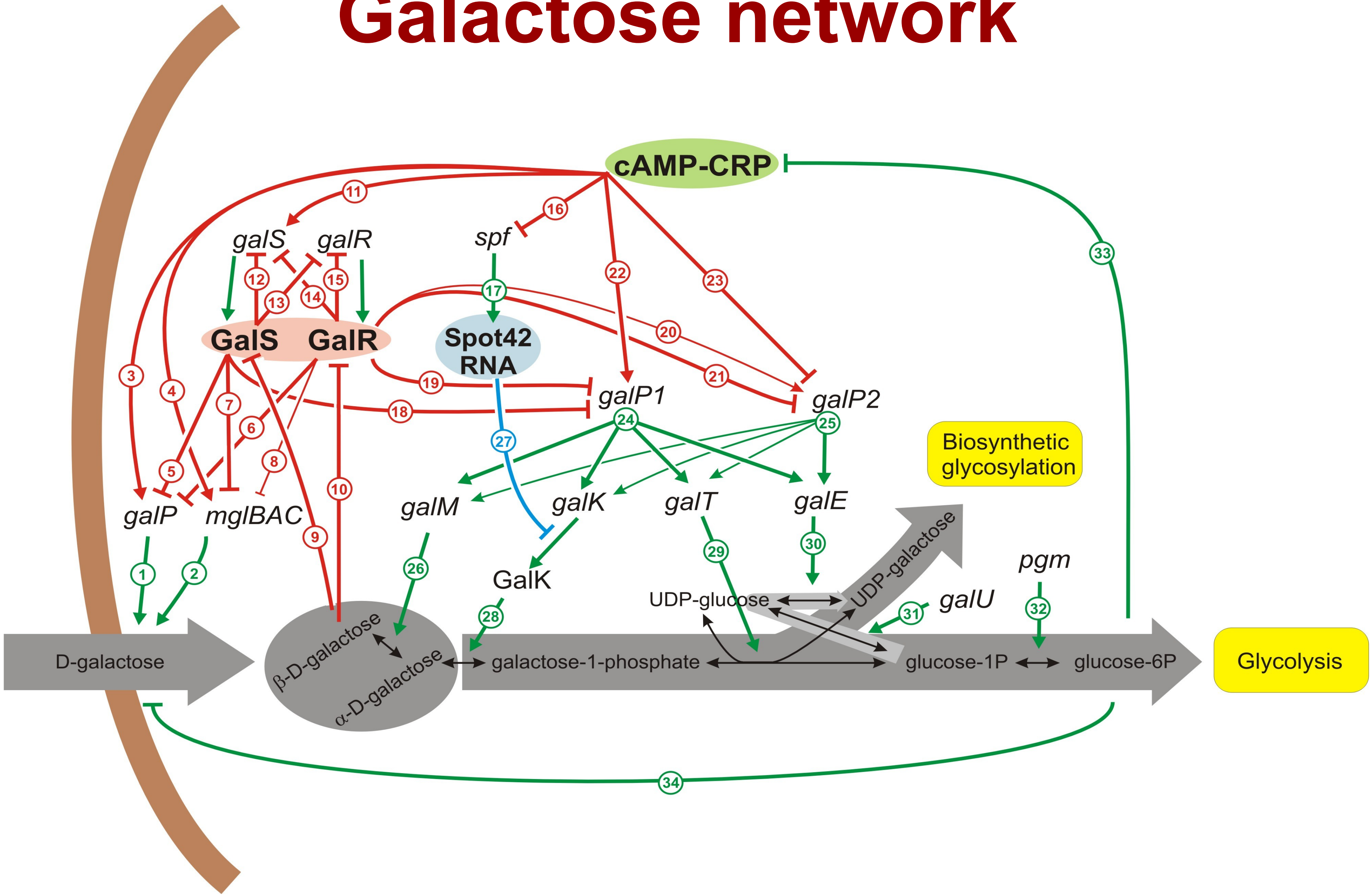
Why two regulators?

Galactose network



Two input signals: galactose, cyclic AMP

Galactose network

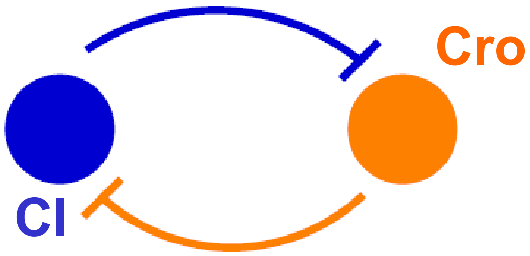


Szabolcs Semsey, Sandeep Krishna, Kim Sneppen, Sankar Adhya (2007)
Signal integration in the galactose network of Escherichia coli, Mol. Microbiol. 65, 465.

"Standard model" of λ

Ptashne, A Genetic Switch: Phage Lambda Revisited

Ptashne & Gann, Genes and Signals



- Simple positive feedback (A represses B; B represses A)
- Net result of positive feedback:

  Two states:

  1. Lytic (CI low, Cro high)
  2. Lysogenic (CI high, Cro low)

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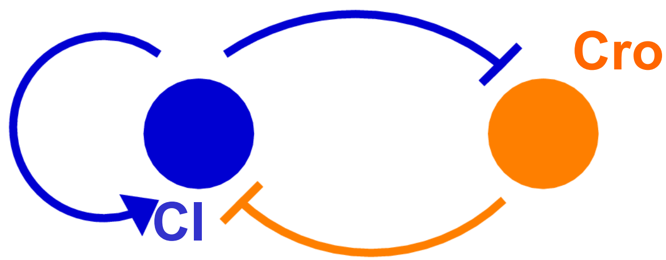

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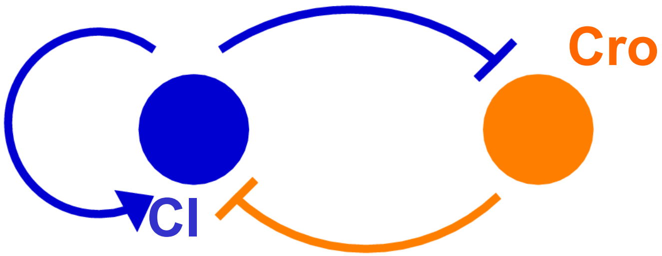
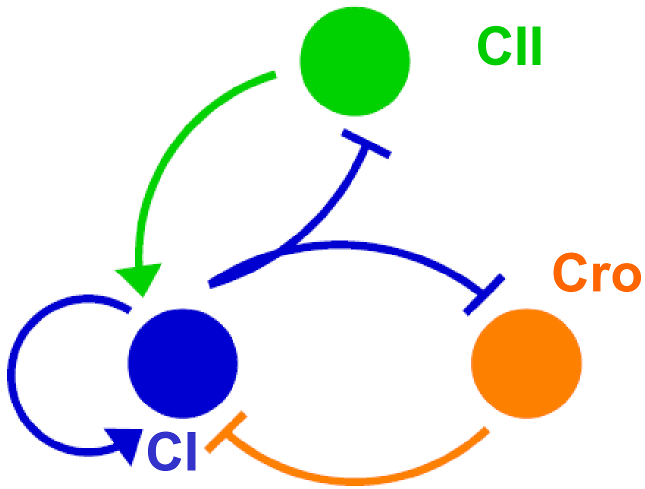


- If *cI* promoter (PRM) needs activation by CI, and *cro* promoter (PR) is constitutive,
  - how is lysogeny established?

“Standard model” of λ

Ptashne, A Genetic Switch: Phage Lambda Revisited

Ptashne & Gann, Genes and Signals



•If *cI* promoter (PRM) needs activation by CI, and *cro* promoter (PR) is constitutive,

- how is lysogeny established?

•*cro* promoter, PR, also produces CII, which activates production of CI from PRE

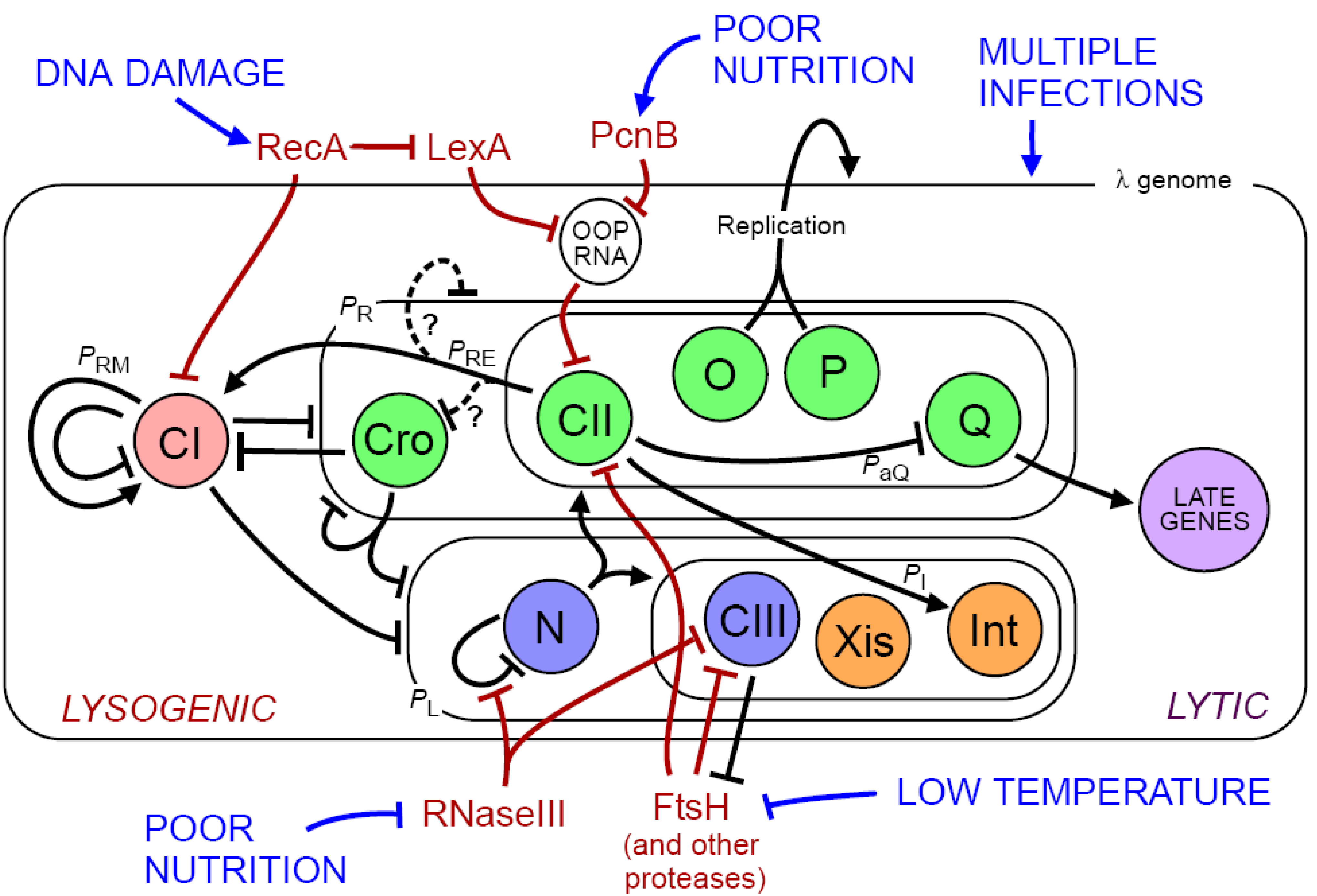
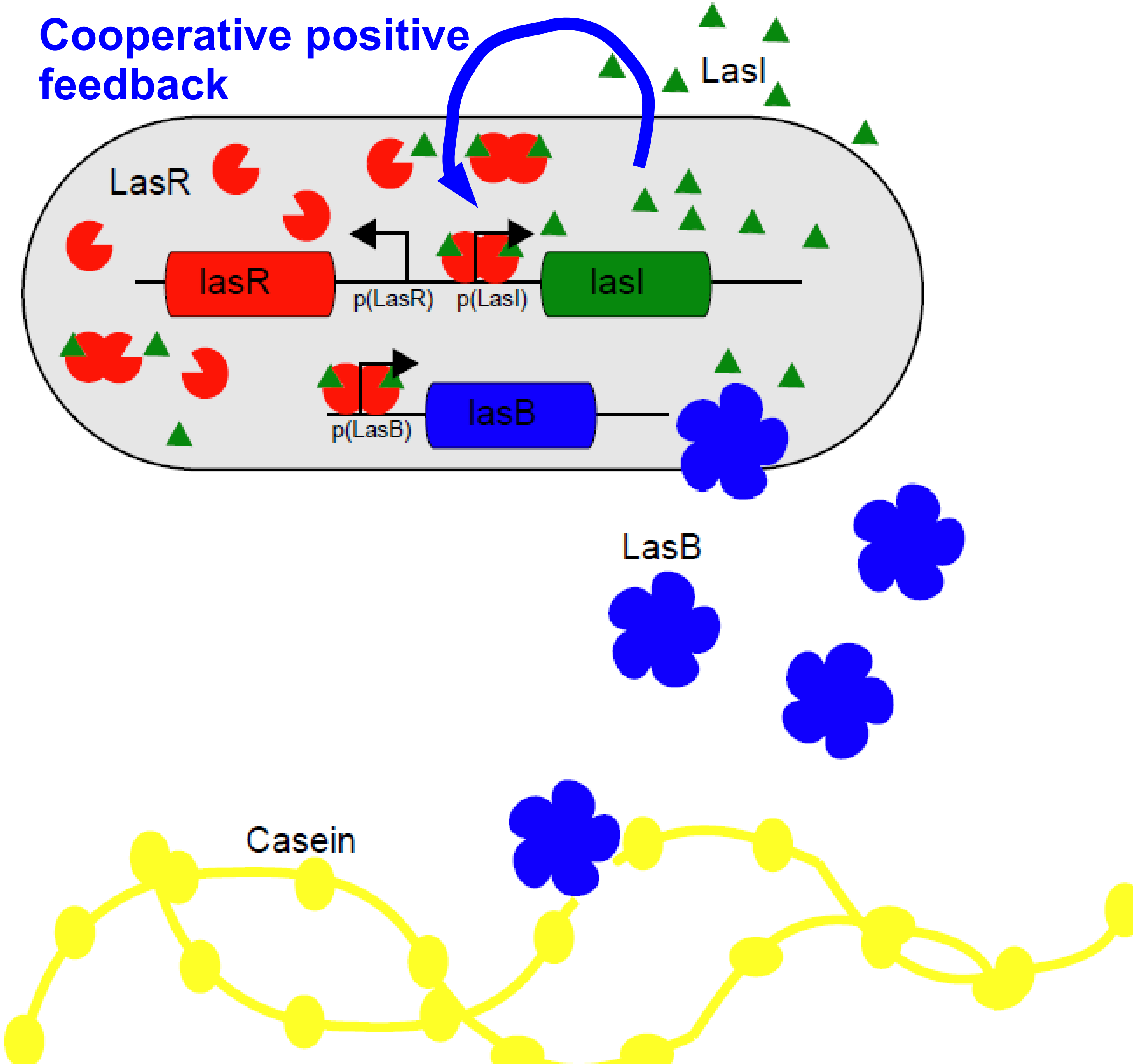
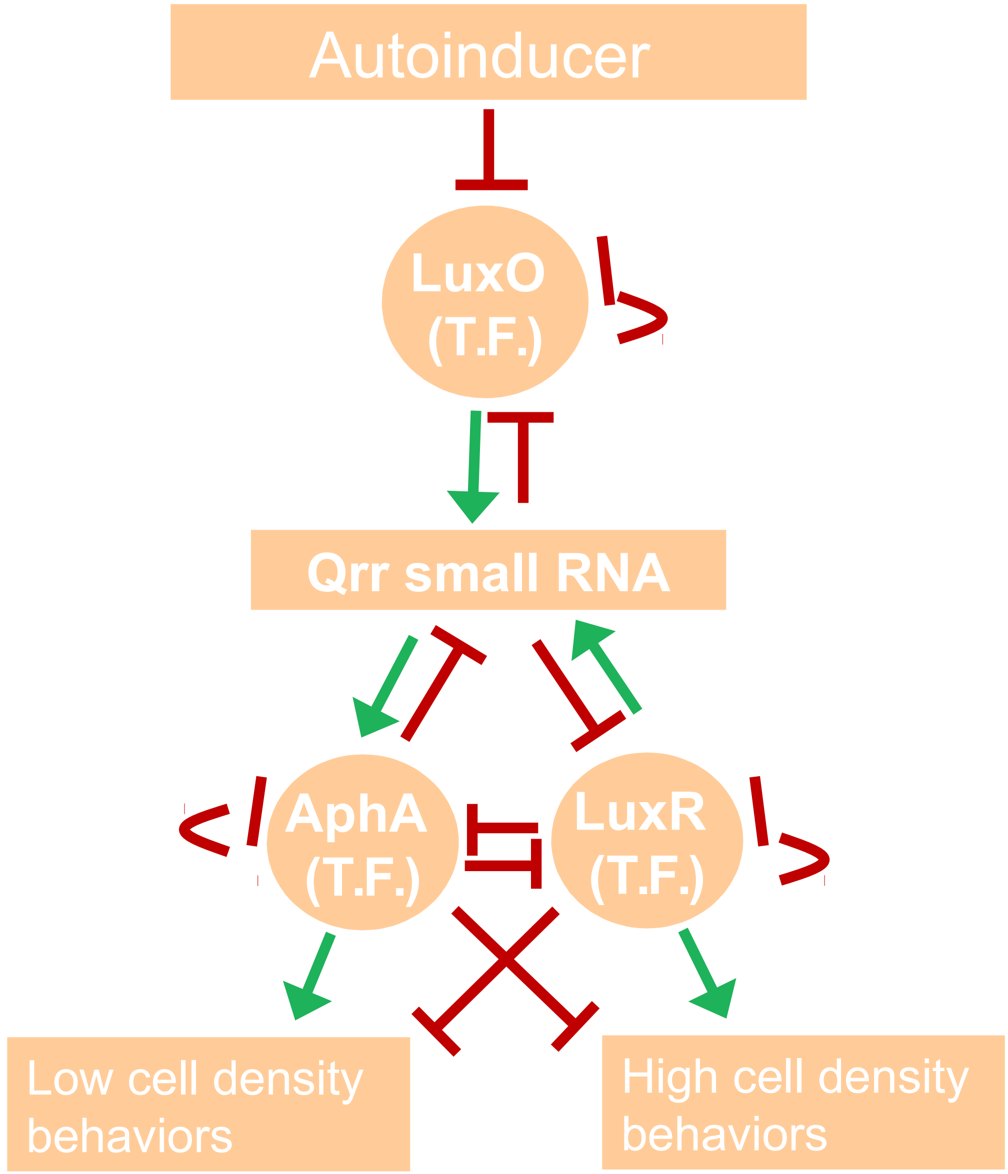


Image courtesy Keith Shearwin, Adelaide Univ.

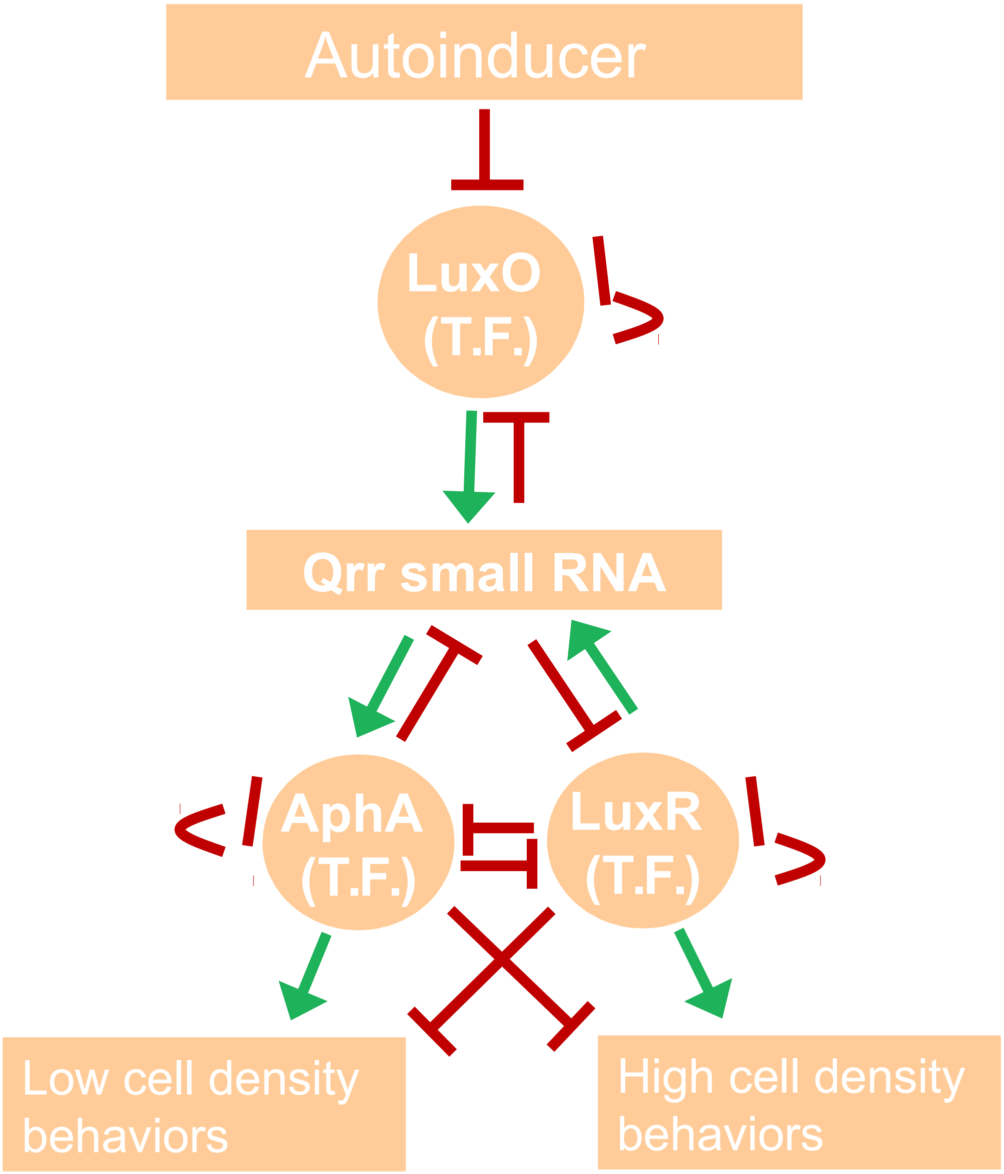
Quorum sensing in *P. aeruginosa*



Quorum sensing in *V. harveyi*



Quorum sensing in *V. harveyi*



Further Reading:

Negative feedback loops involving small regulatory RNAs precisely control the Vibrio harveyi quorum-sensing response
KC Tu, T Long, SL Svenningsen, NS Wingreen, BL Bassler (2010)
Molecular cell 37 (4), 567-579

Gene dosage compensation calibrates four regulatory RNAs to control Vibrio cholerae quorum sensing
SL Svenningsen, KC Tu, BL Bassler (2009) The EMBO journal 28, 429-439

A small-RNA-mediated negative feedback loop controls quorum-sensing dynamics in Vibrio harveyi. KC Tu, CM Waters, SL Svenningsen, BL Bassler (2008)
Molecular microbiology 70 (4), 896-907

A negative feedback loop involving small RNAs accelerates Vibrio cholerae's transition out of quorum-sensing mode
SL Svenningsen, CM Waters, BL Bassler (2008) Genes & development 22, 226-238

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