IV Master in Biophysics
Universidad Autónoma de Madrid
Oct 26 – Nov 8/2006

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Stochastic dynamics

Evolutionary Systems Biology Lab

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SPANISH NATIONAL CANCER CENTRE

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day IV


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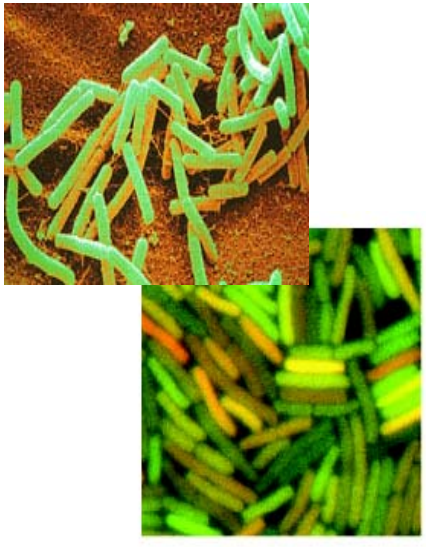
Prokaryotic gene expression



Noise associated to translational efficiency rather than transcriptional efficiency (translational bursting)

$$\text{Fano} = 1 + \frac{k_P}{\delta_R}$$

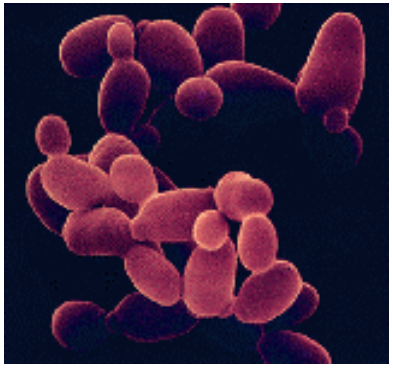
Inefficient translation → Less noise

Other sources of variability (external to gene expression): external noise

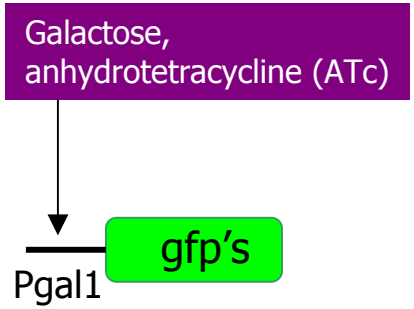
Two reporter strategy: Two (almost) identical fluorescence proteins Simultaneously expressed from same promoters.

As the rate of transcription decrease protein noise increase from finite-number effects.
Low molecular abundances → limit precision of gene expression

Eukaryotic gene expression



yeast



Several strategies
to modify transcription
and translation efficienty

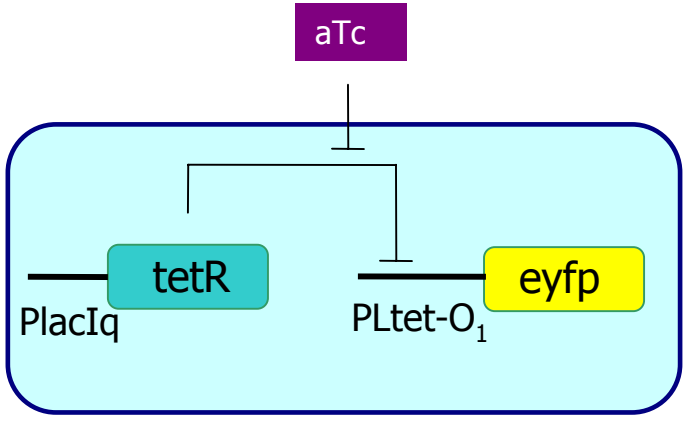
Main conclusions:

- translational bursting as in prokaryotes

- transcriptional bursting: slow transitions between promoters states: chromating remodelling, etc. (to be discussed in detail in one of the student presentations)

Information flow and noise in a genetic cascade

Circuit 1



INPUT anhydrotetracycline (aTc)

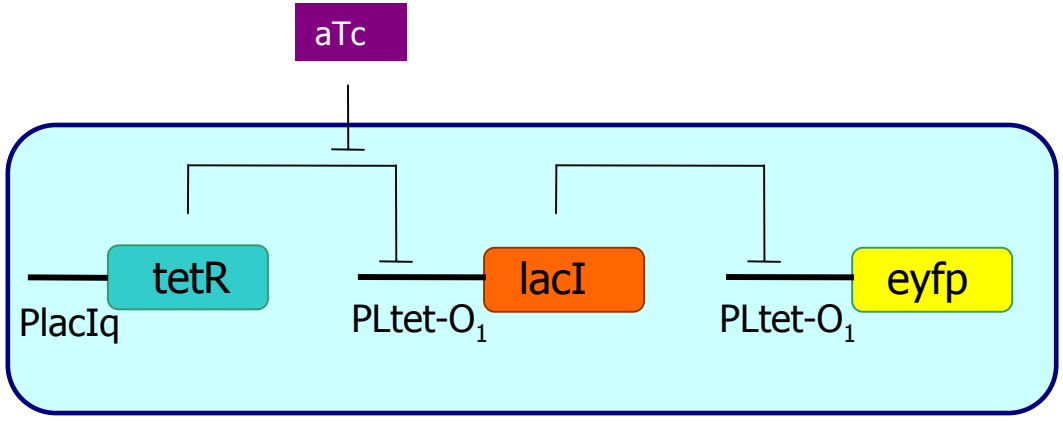
OUTPUT enhanced yellow fluorescence protein (EYFP)

Some Details: cell cycle → ~45 min
30-50 different concentrations of aTc used
measurements in cytometer

Circuit elements: Tet repressor
Lac repressor
λ repressor
ALL three highly stable proteins → Decay ~ cell cycle time

Information flow and noise in a genetic cascade

Circuit 2



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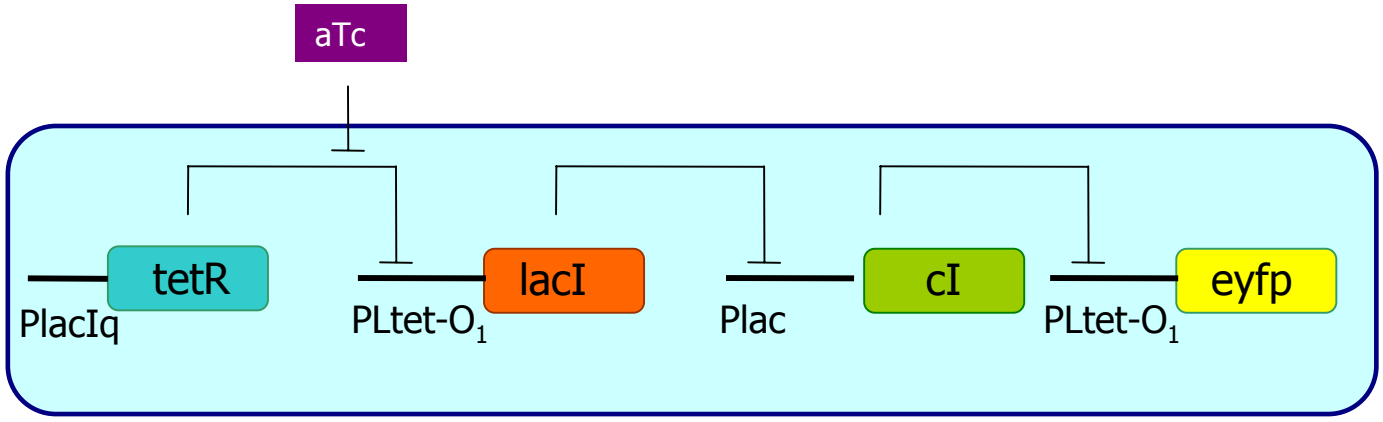
Information flow and noise in a genetic cascade

Circuit 3



INPUT anhydrotetracycline (aTc)

OUTPUT enhanced yellow fluorescence protein (EYFP)

Some Details: cell cycle → ~45 min
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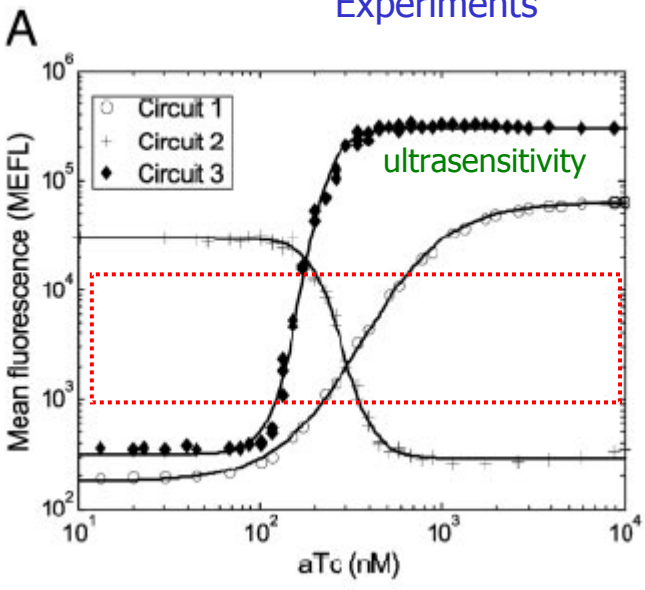
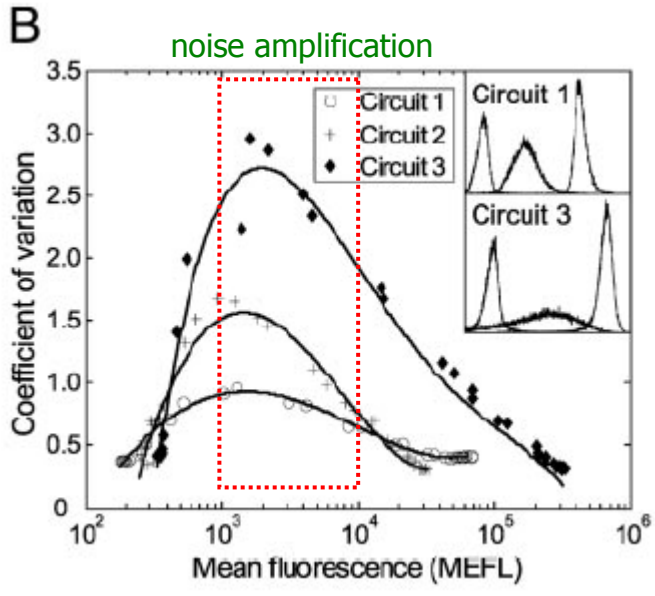
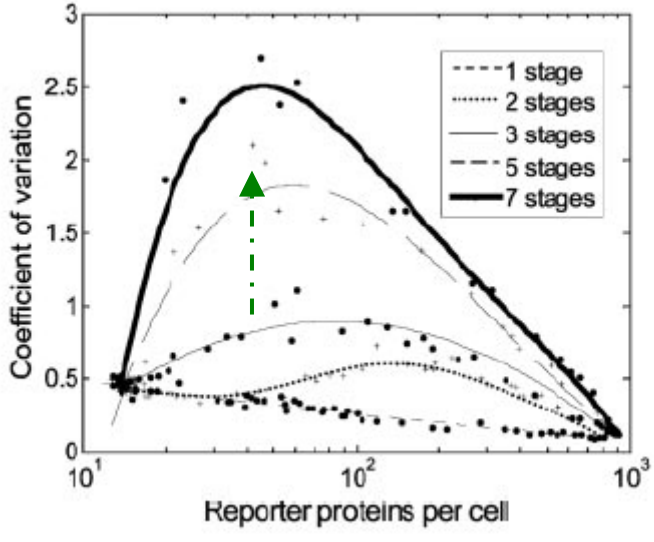
Circuit elements: Tet repressor
Lac repressor
λ repressor
ALL three highly stable proteins → Decay ~ cell cycle time

Steady state transfer curve; ultrasensitivity

Experiments

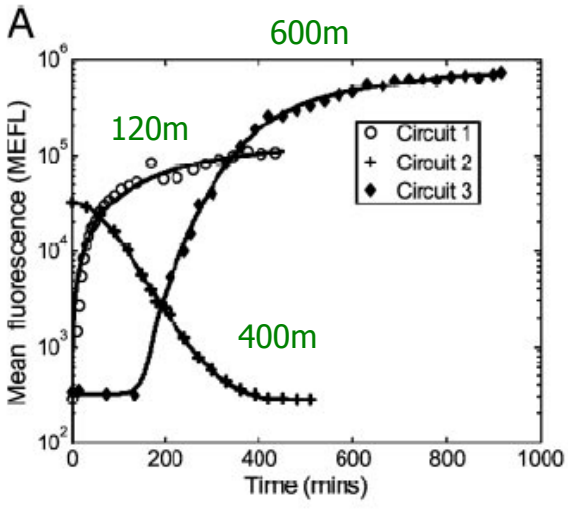


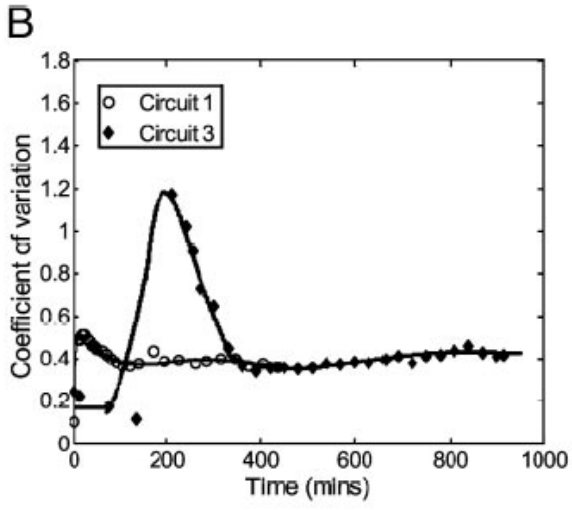


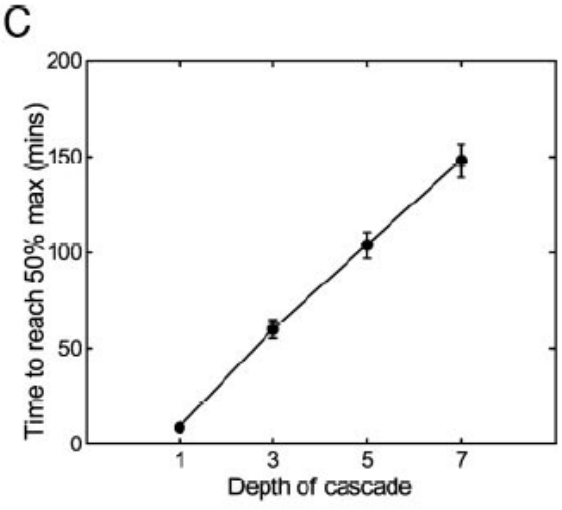


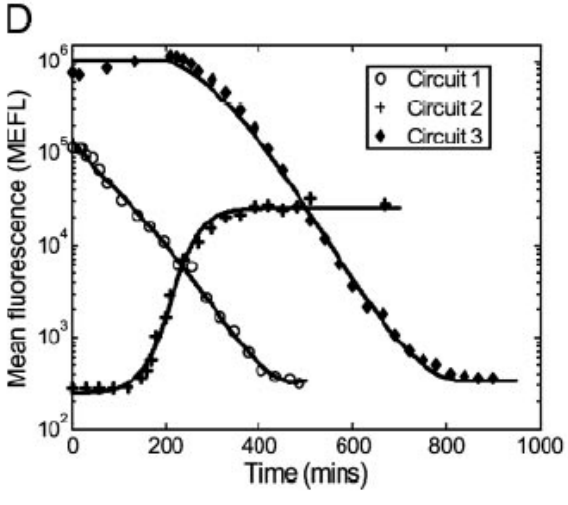
Simulations

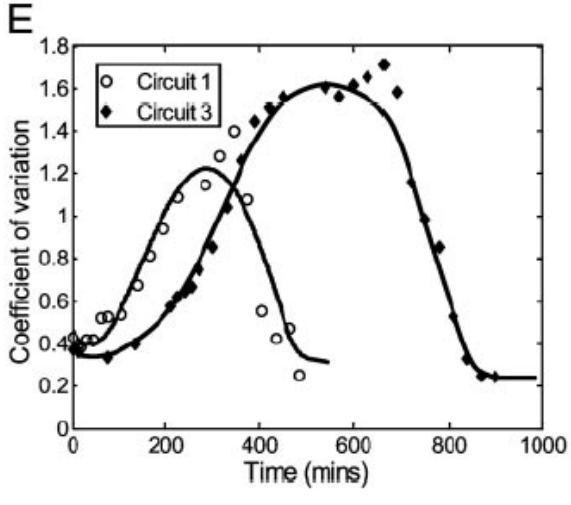
Delayed response

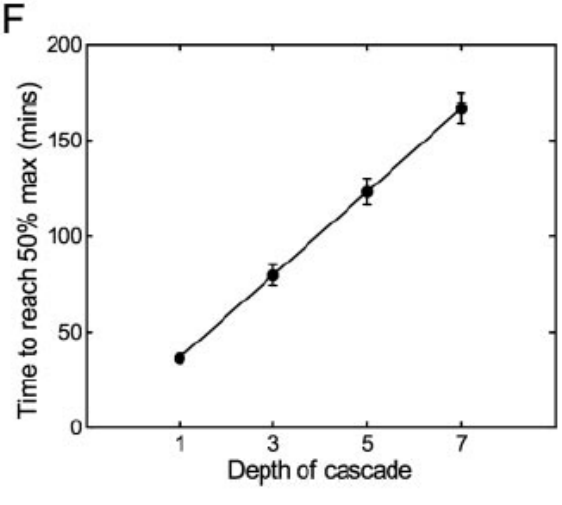




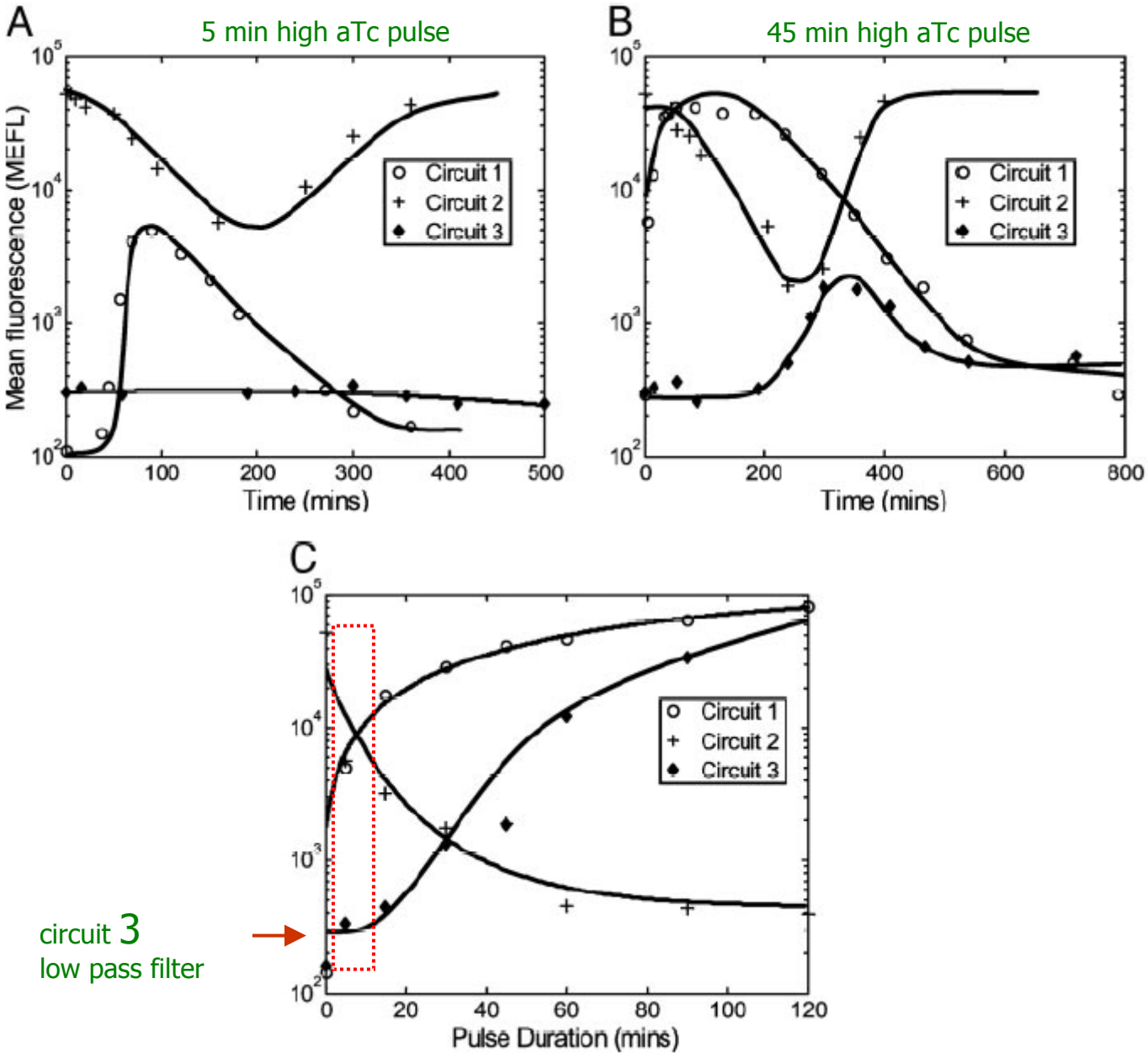








Low-pass filtering



References

Prokaryotic noise

- Intrinsic noise: Regulation of noise in the expression of a single gene
  Ozbudak E. M. *et al*, Nat. Gen. **31**, 69 (2002)
- Intrinsic/extrinsic noise: Stochastic gene expression in a single cell
  Elowitz M. B. *et al,* Science **297**, 1183 (2002)

Eukaryotic noise

- Intrinsic noise: Noise in eukaryotic gene expression
  Blake W. J. et al, Nature **422**, 633 (2003)

* - Intrinsic/extrinsic: Control of stochasticity in eukaryotic gene expression
  Raser J. M. and O'Shea E. K., Science **304**, 1811 (2004)

Noise flow

* - Ultrasensitivity and noise propagation in a synthetic transcriptional cascade
  Hooshangi S. *et al*, PNAS **102**, 3581 (2005)
* - Gene regulation at the single-cell level
  Rosenfeld N. et al, Science **307**, 1962 (2005)
- Noise propagation in gene networks
  Pedraza J. M., and van Oudenaarden A., Science **307**, 1965 (2005)

¡Hasta la próxima!

* student presentation