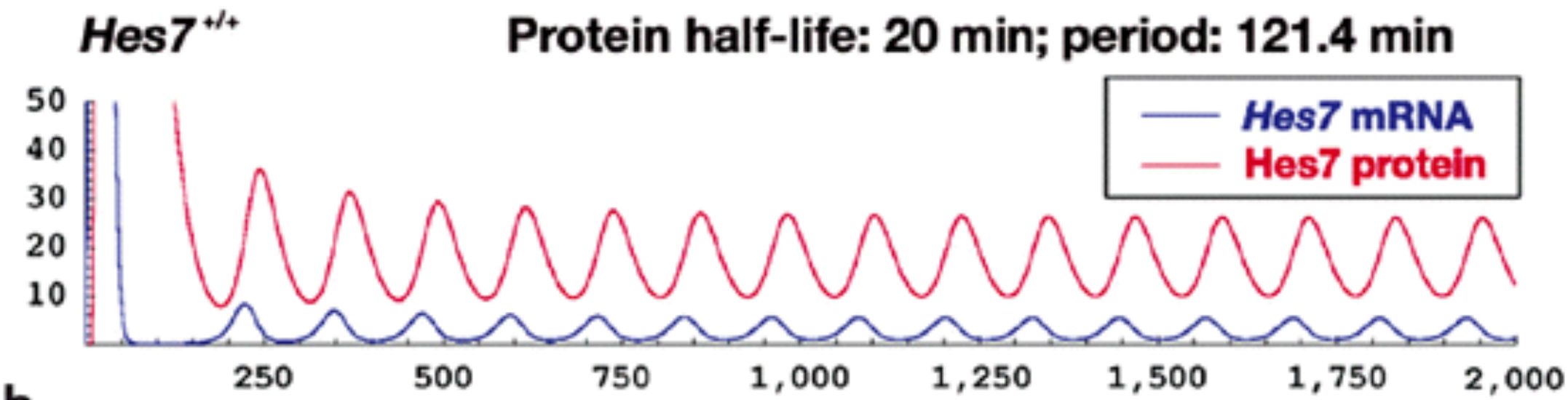
a



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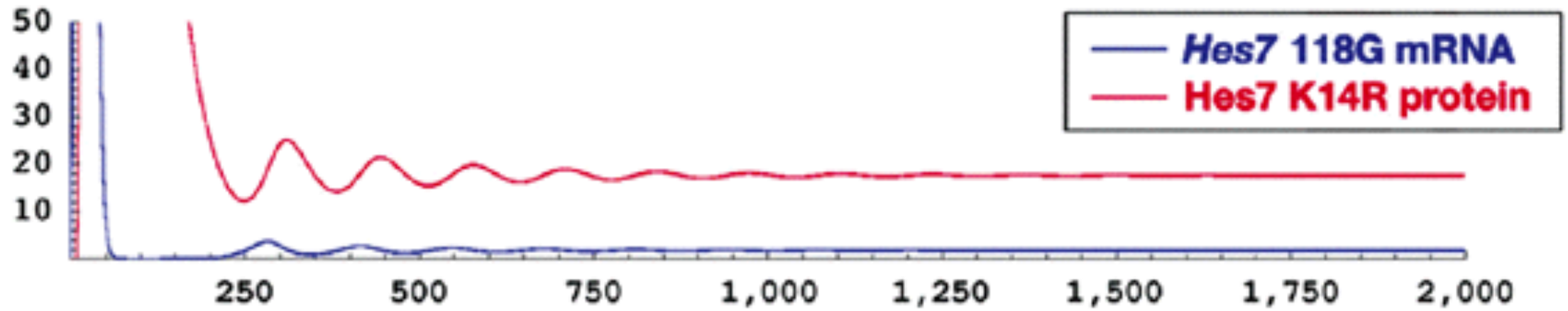
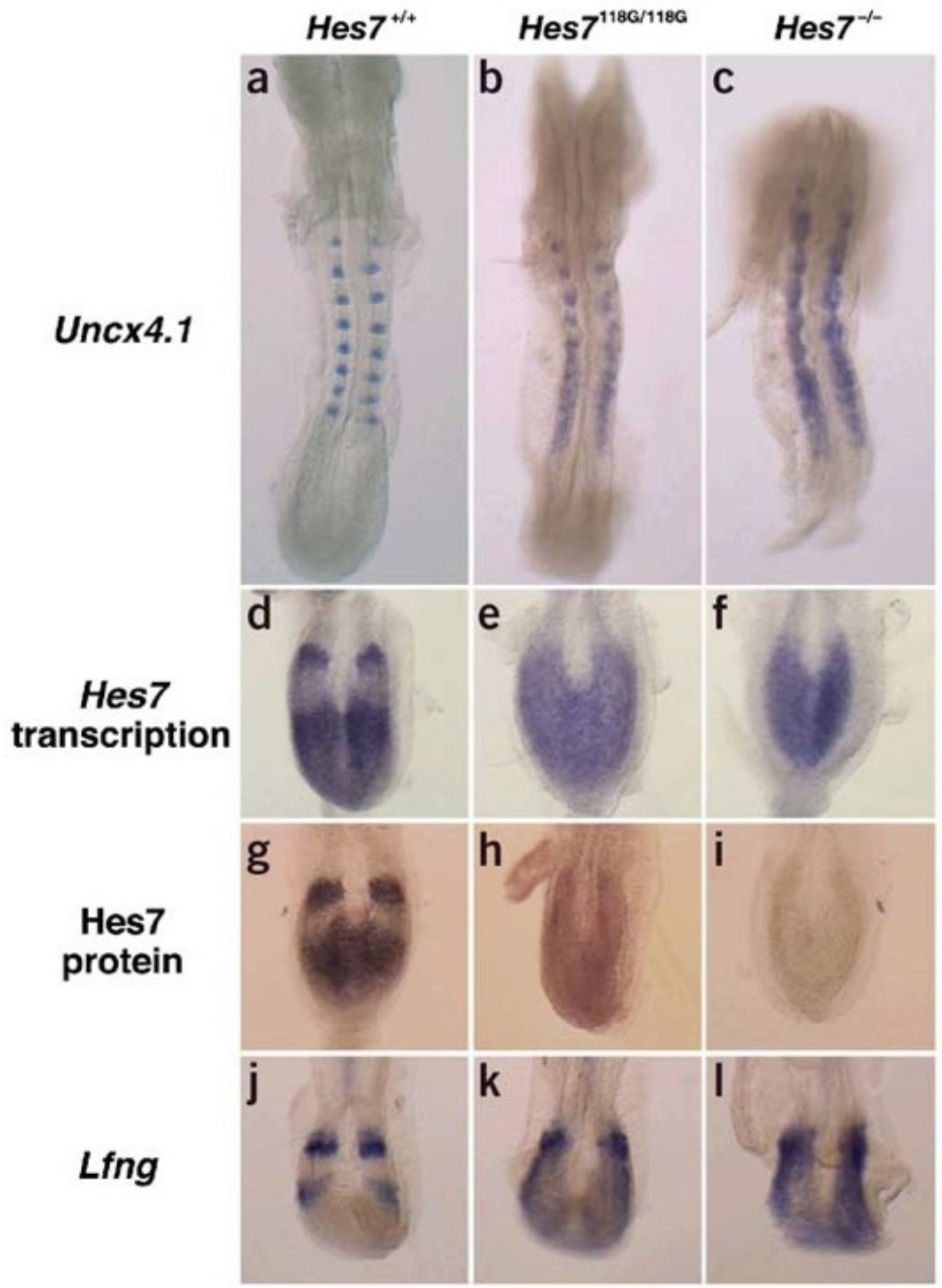
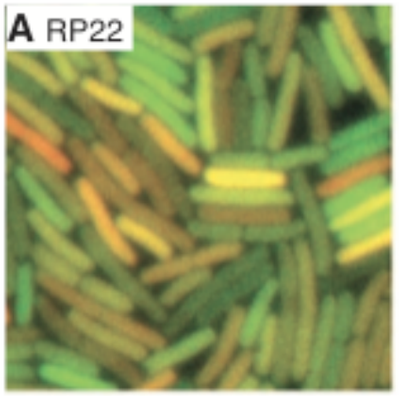
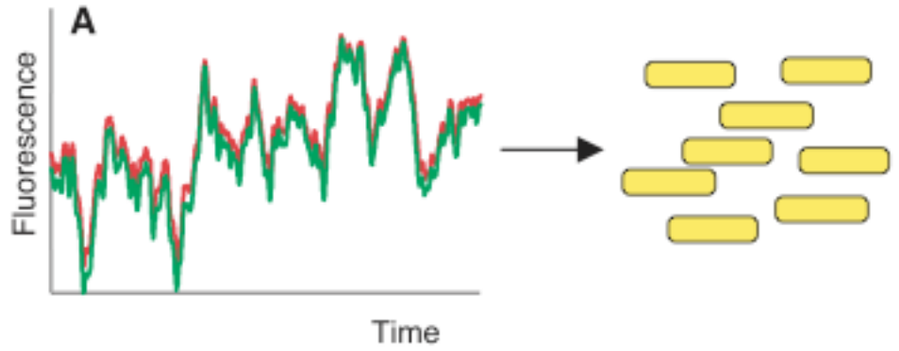
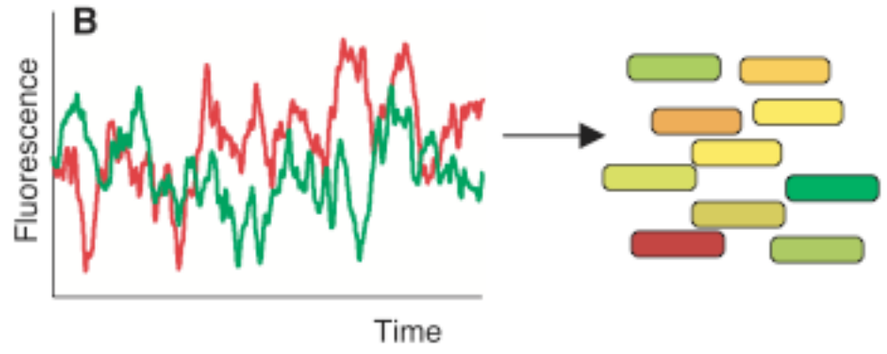


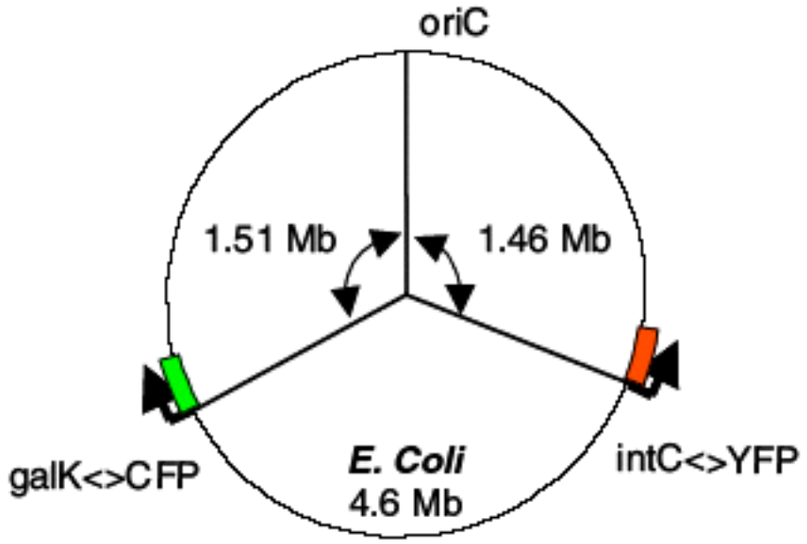
Hirata et al, Nat. Gen. 36, 750 (2004)


Hes7+/+
Hes7118G/118G
Hes7−/−
a
b
c
Uncx4.1
d
e
f
Hes7
transcription
g
h
i
Hes7
protein
j
k
l
Lfng









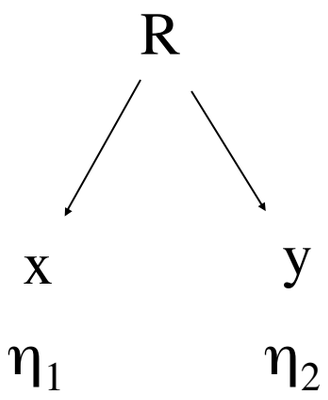
$$\eta = \frac{< F_i^2 > - < F_i >^2}{< F_i >^2}$$

- two colours of GFP controlled by identical regulatory sequences in the same cell
- if deterministic one colour
- if stochastic mixed colours

Michael B. Elowitz, Arnold J. Levine,Eric D. Siggia, Peter S. Swain

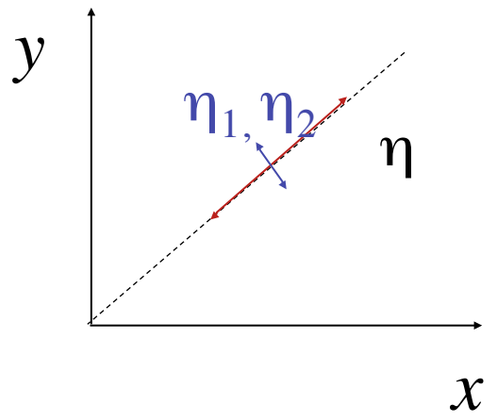
Stochastic Gene Expression in a Single Cell

SCIENCE VOL 297 16 AUGUST 2002



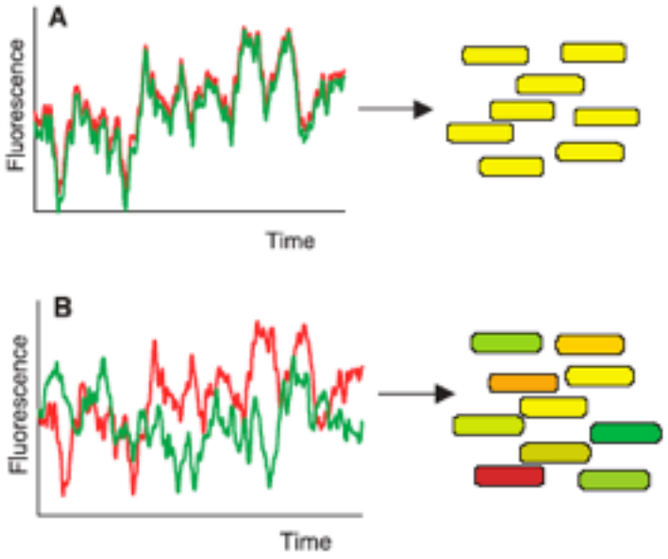
external signal

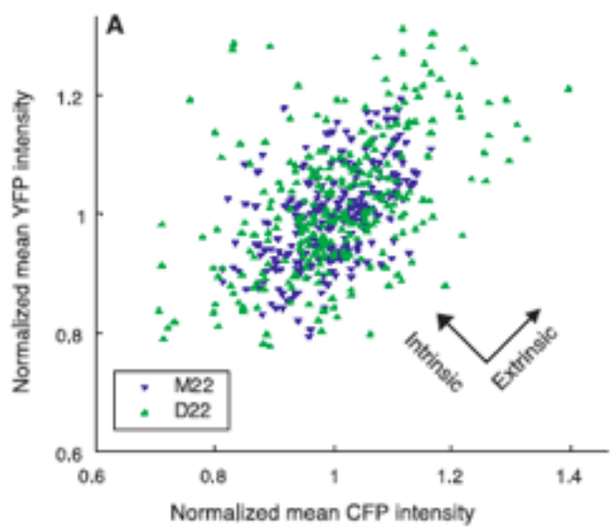
products of two different genes regulated by R



$$\dot{x} = f_1(R)\eta(t)\eta_1(t) - kx$$

$$\dot{y} = f_1(R)\eta(t)\eta_2(t) - ky$$





- not all noise extrinsic
- some intrinsic (why?)

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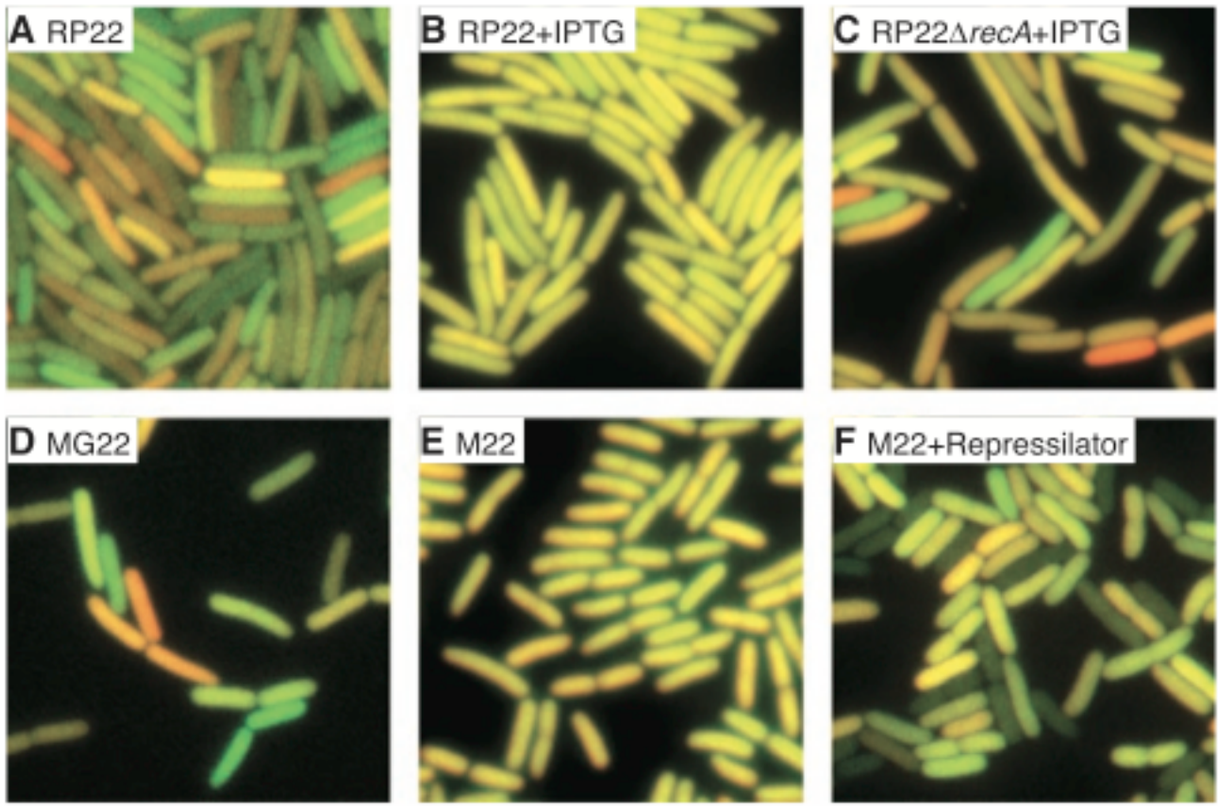

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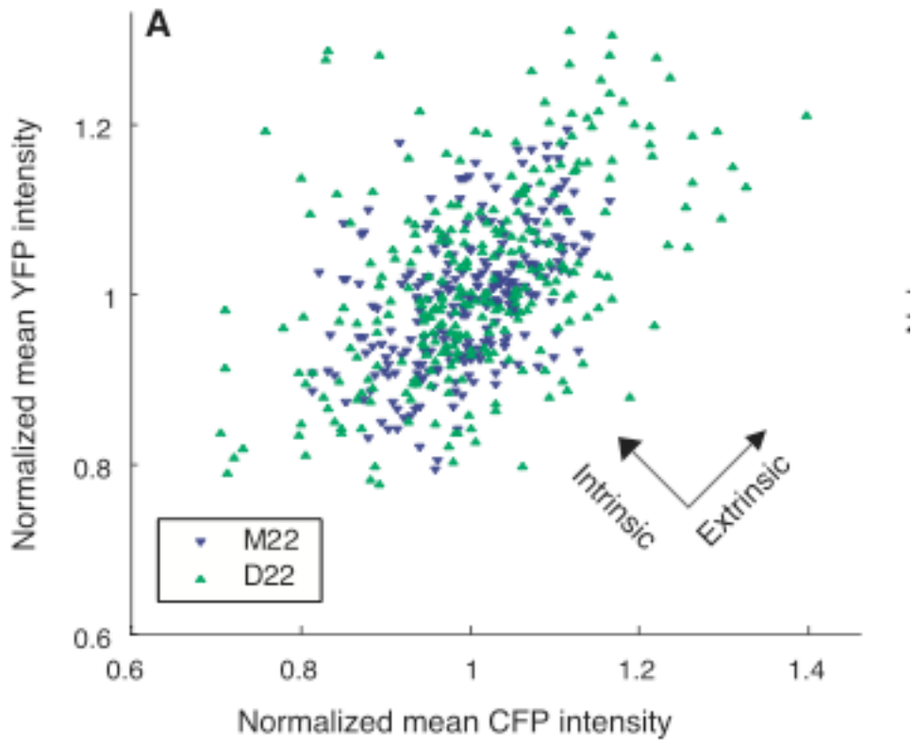
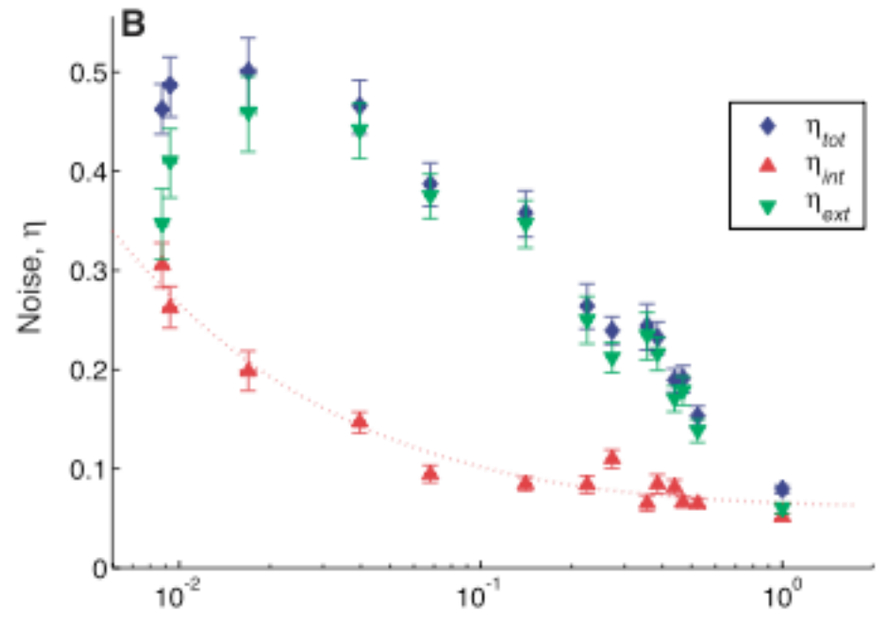
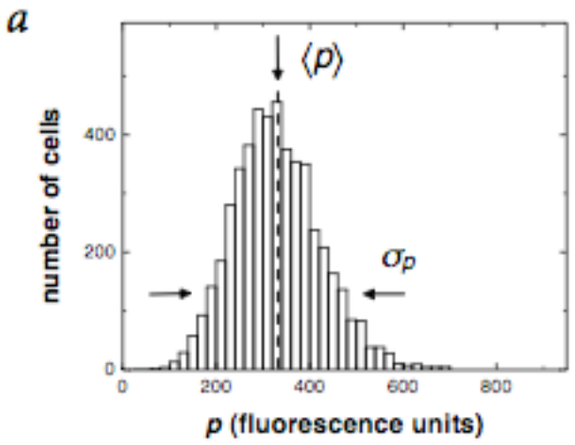




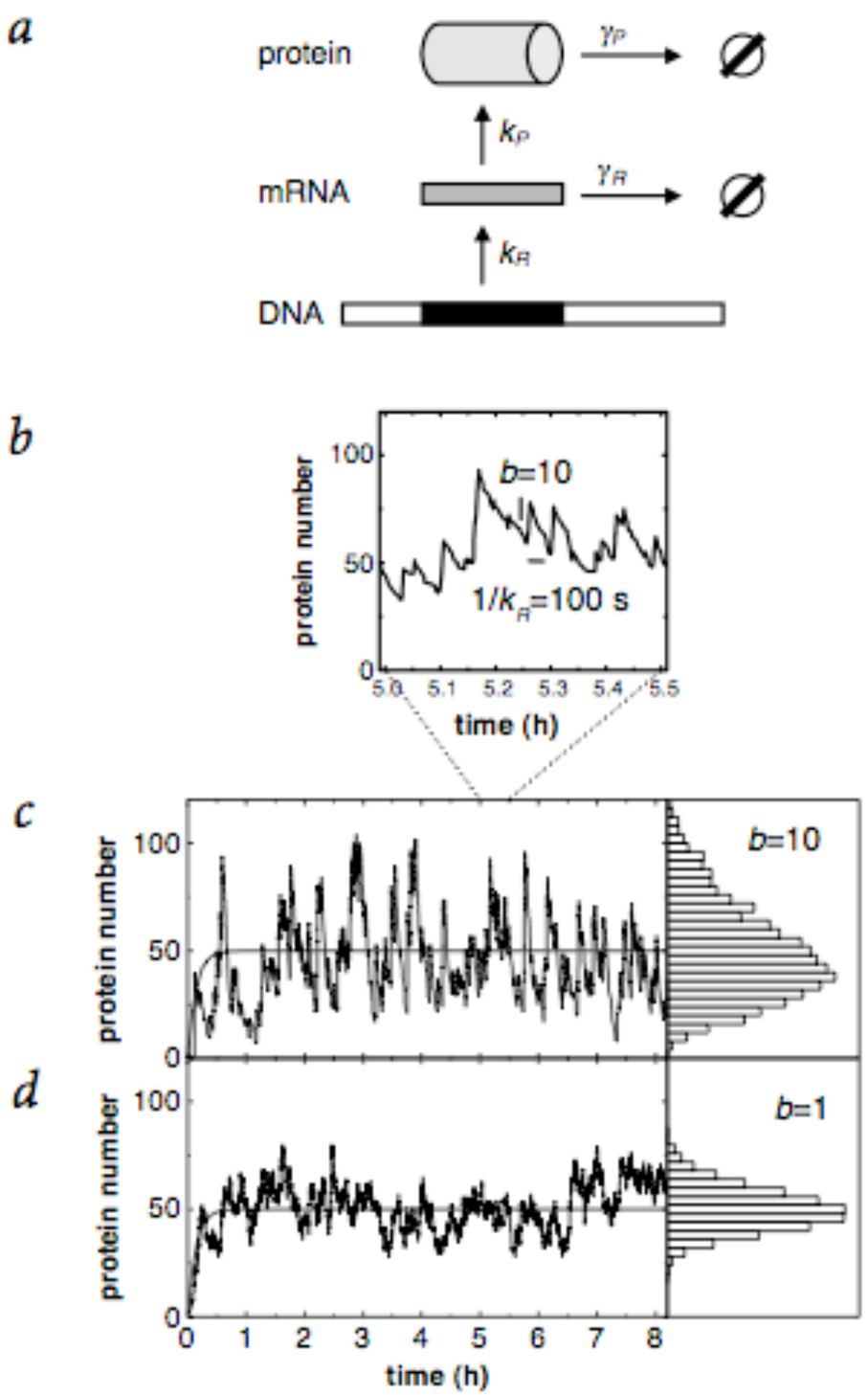
rate of transcription in strain M22 (recA+, lacI–), with LacI supplied by plasmid pREP4

small copy numbers → **more noise**



$$\frac{\langle \delta p^2 \rangle}{\langle p \rangle} \equiv \frac{\sigma_p^2}{\langle p \rangle} = 1 + \frac{b}{1+\phi}$$

- translational bursts
- explain this result



Ertugrul M. Ozbudak, Mukund Thattai, Iren Kurtser, Alan D. Grossman & Alexander van Oudenaarden

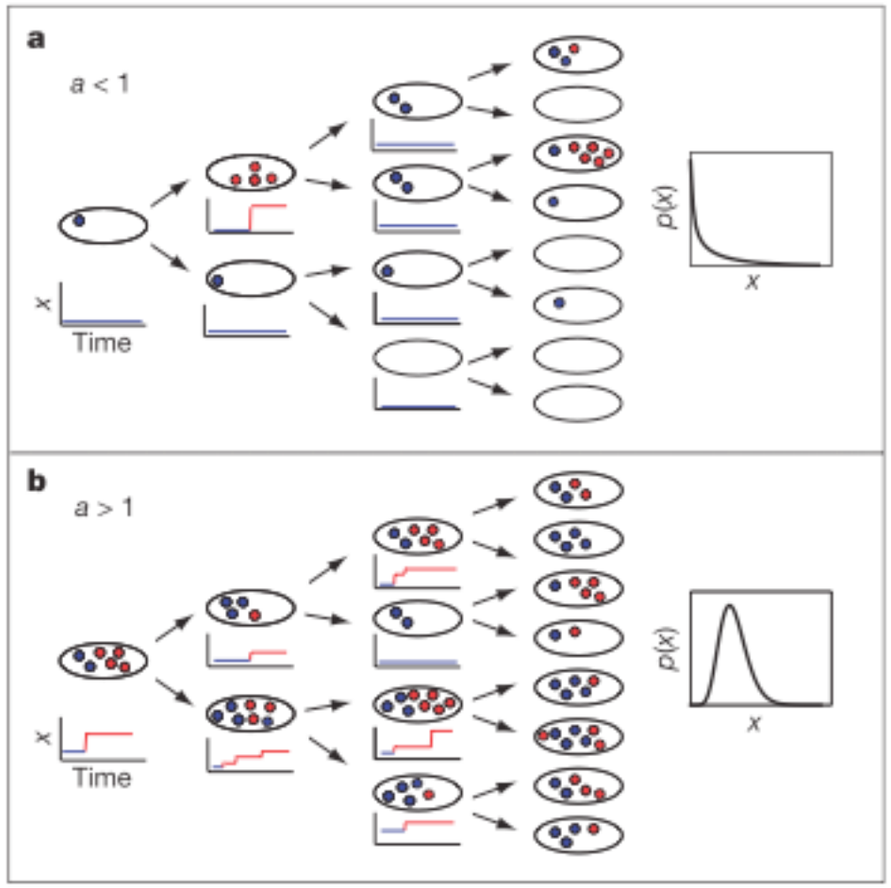
Regulation of noise in the expression of a single gene

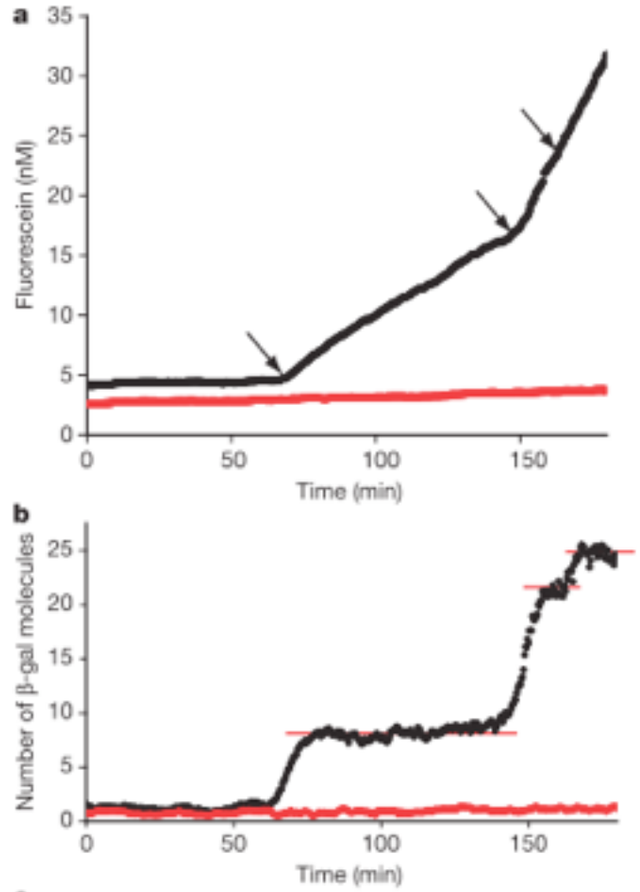
nature genetics • volume 31 • may 2002

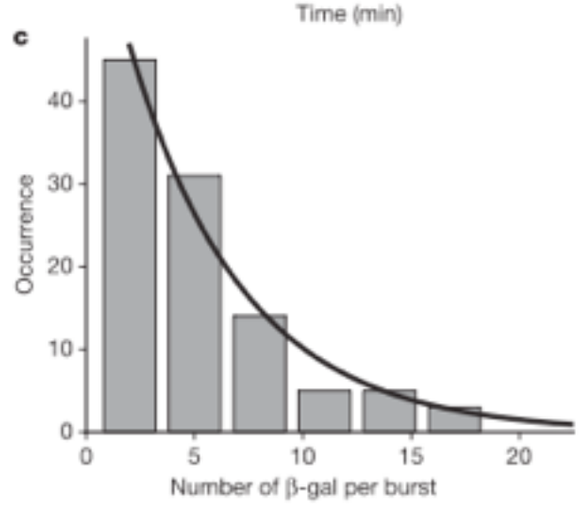
Long Cai, Nir Friedman & X. Sunney Xie

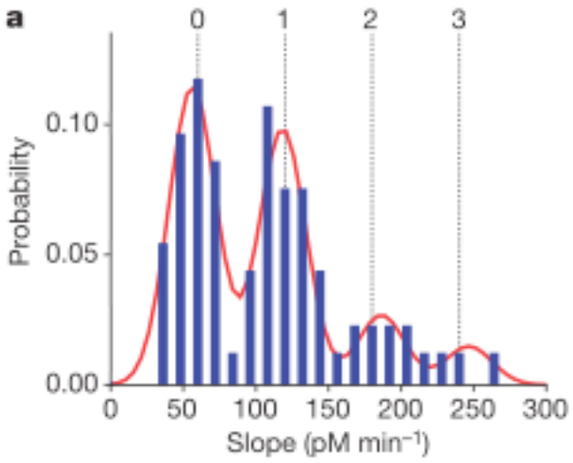
Stochastic protein expression in individual cells at the single molecule level

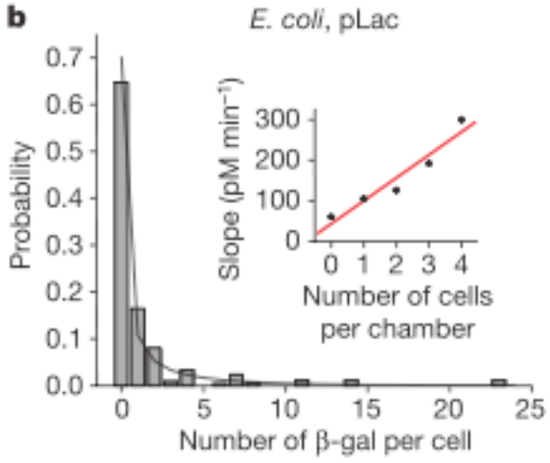
2006 **Nature** VOL 440:358

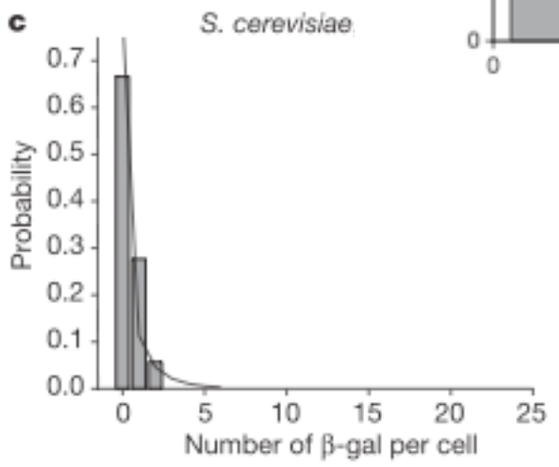


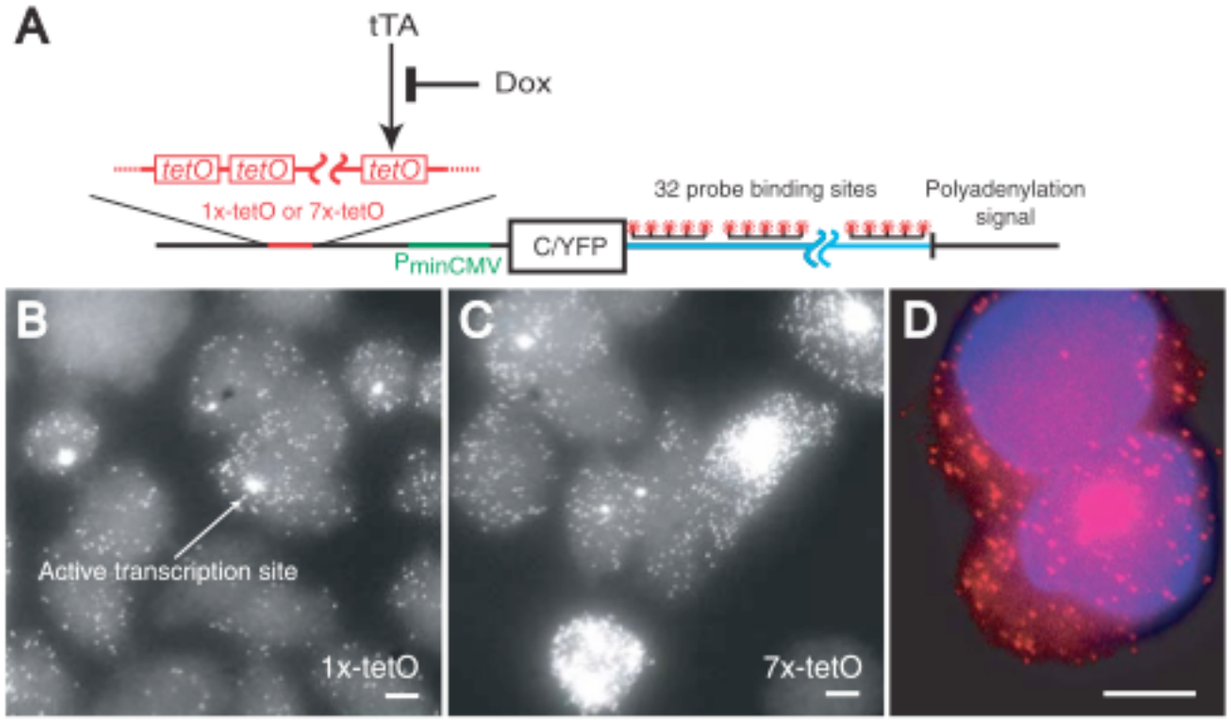






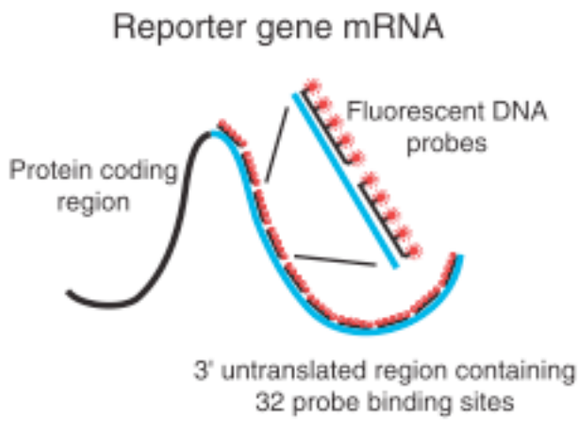


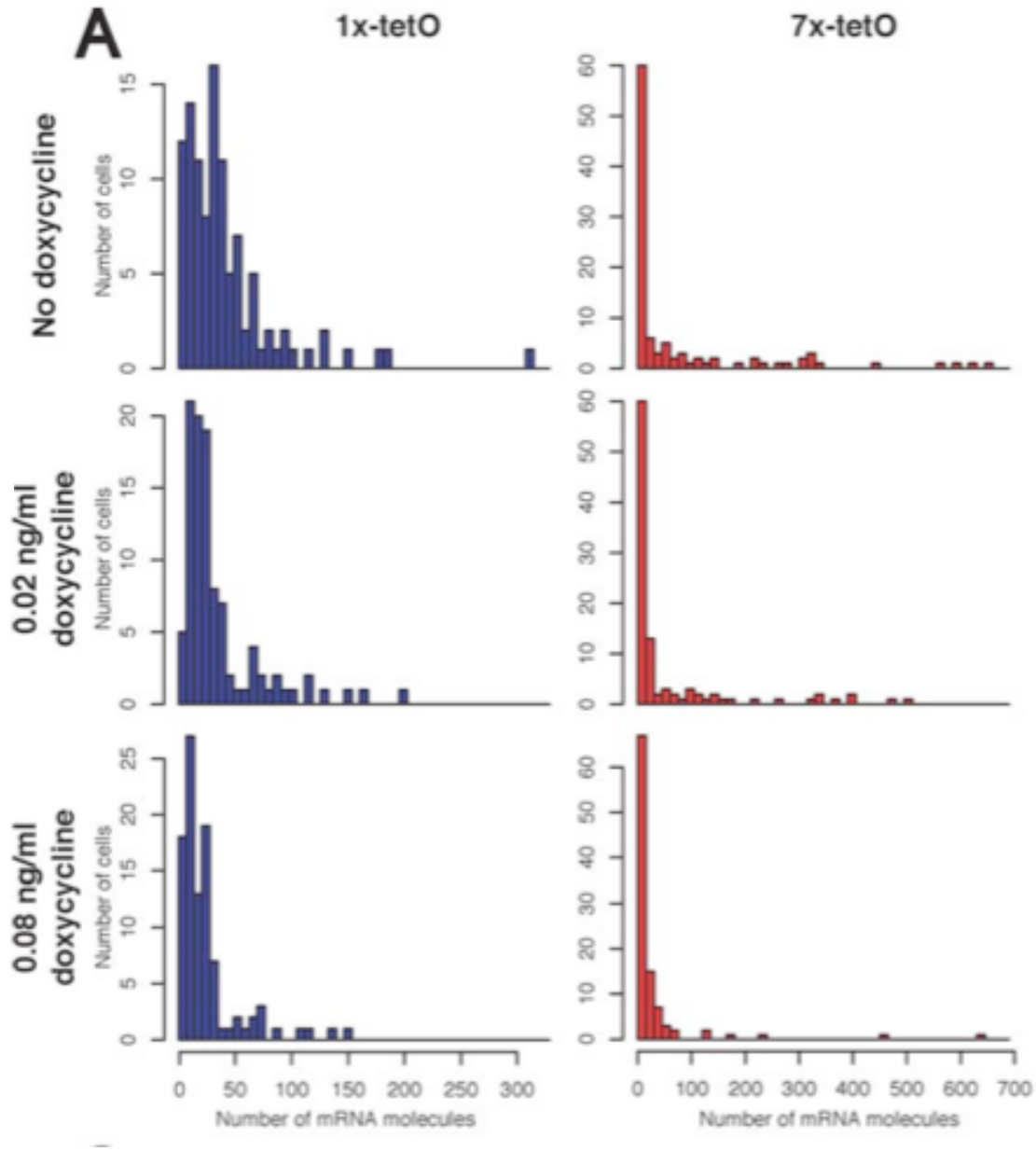




chinese hamster ovary cells

- no longer Poisson-like
- transcriptional bursts



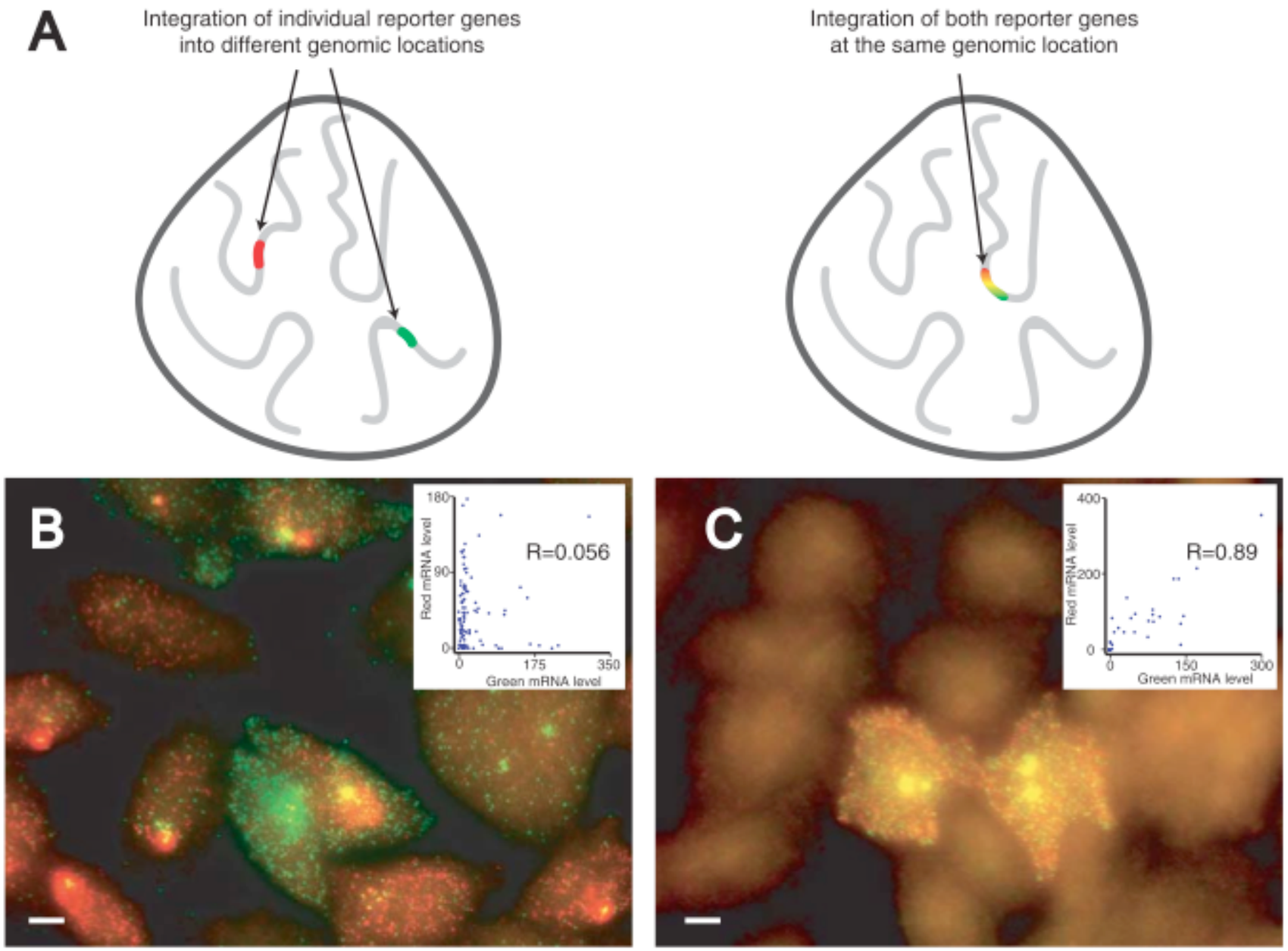


Arjun Raj, Charles S. Peskin, Daniel Tranchina, Diana Y. Vargas, Sanjay Tyagi

Stochastic mRNA Synthesis in Mammalian Cells

PLoS BiologyOctober 2006 | Volume 4 | Issue 10 | e309

- **mechanisms from quantification**



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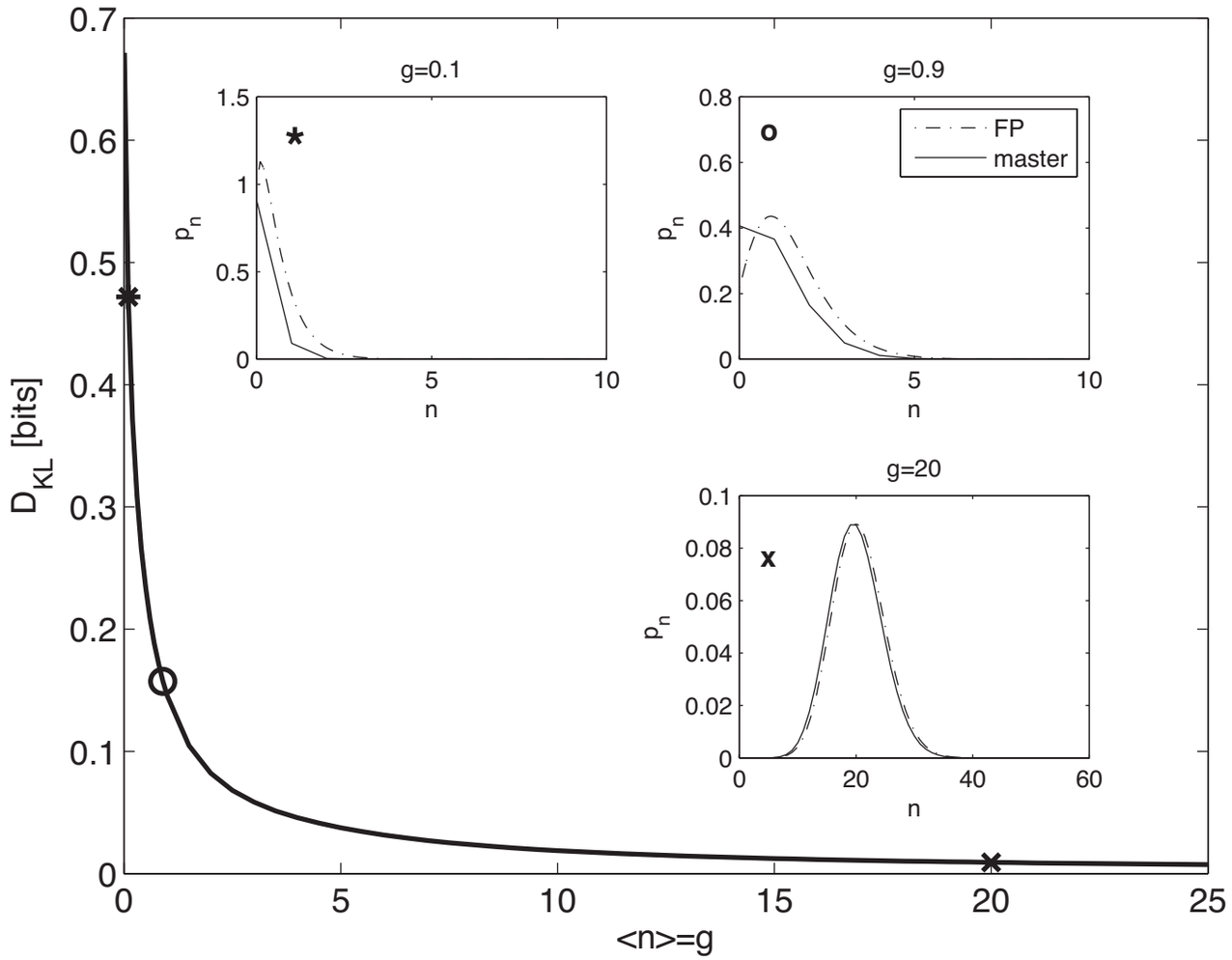
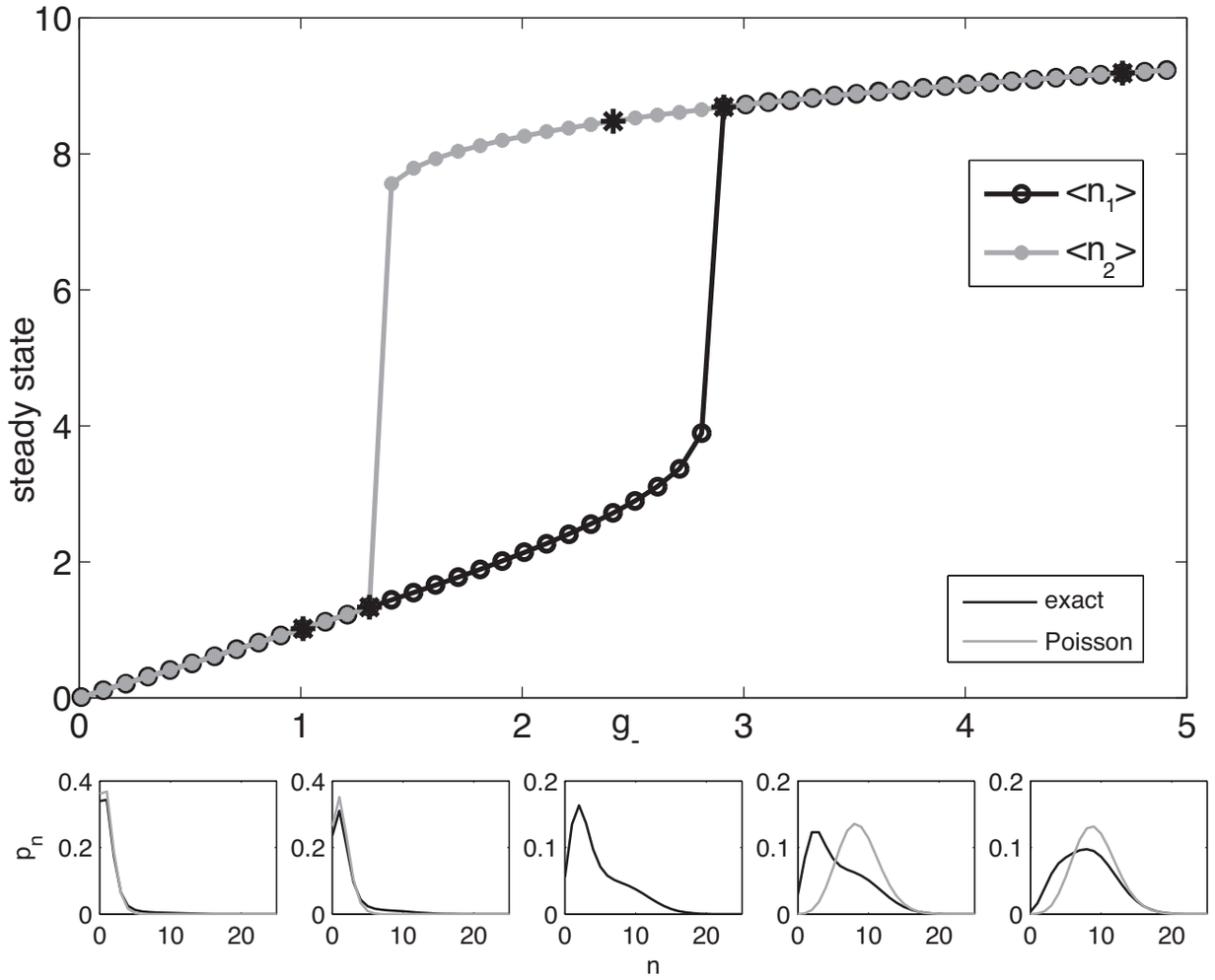
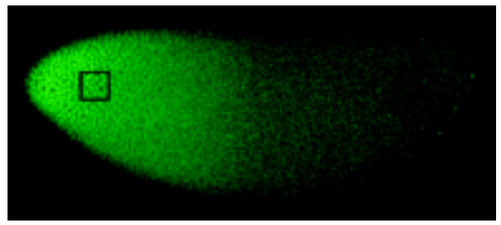


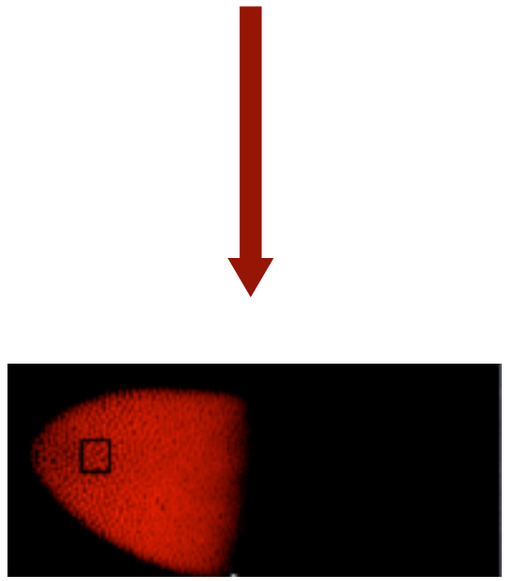
• comparison of FP and master eqn solution for simple birth death process

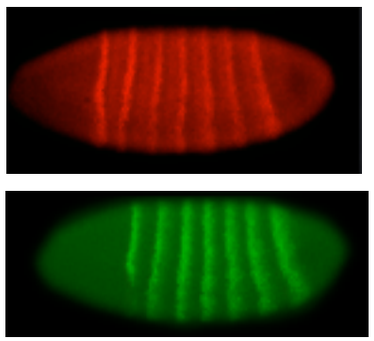


- bimodal distributions - mean is not informative
- small noise approximation fails
- self- activation - super-poissonian statistics
- self- repression - sub-poissonian statistics

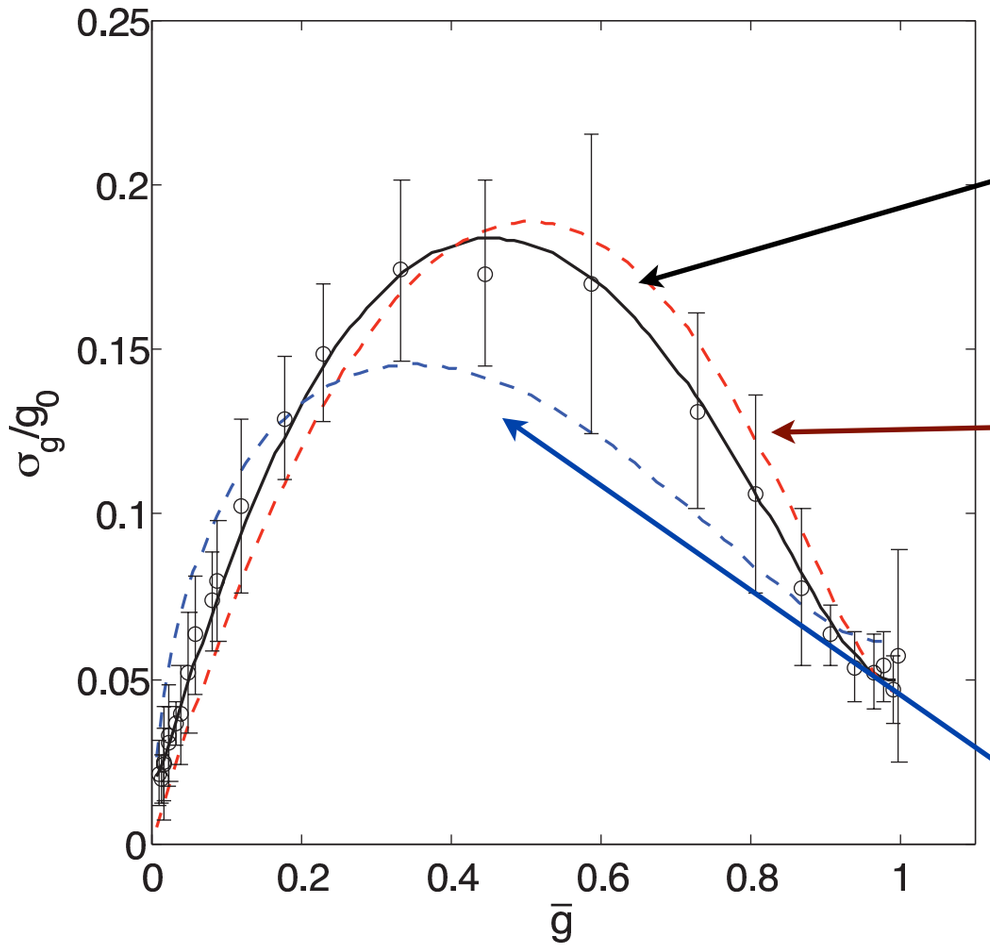
Example: fruit fly development







Comparison of different noise models in the fly



$$\sigma_g^2(c) = \alpha\bar{g}(c) + \beta c(\frac{d\bar{g}(c)}{dc})^2$$

$$\sigma_g^2(c) = \alpha\bar{g}(c)(1-\bar{g}(c))^2 + \beta c(\frac{d\bar{g}(c)}{dc})^2$$

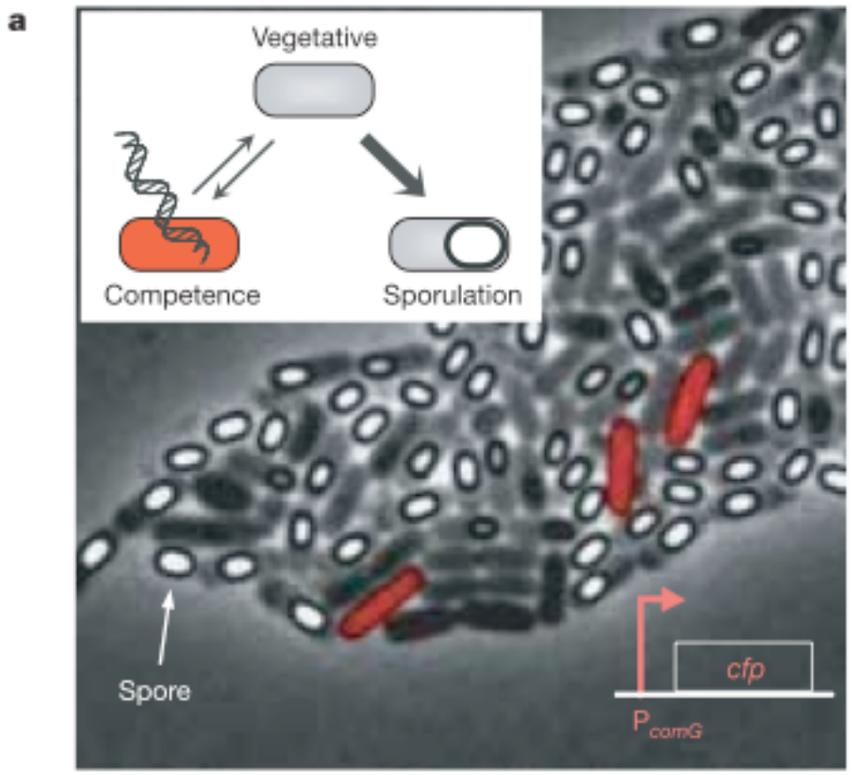
$$\sigma_g^2(c) = \alpha\bar{g}(c) + \beta\bar{g}(c)(1-\bar{g}(c))^2$$

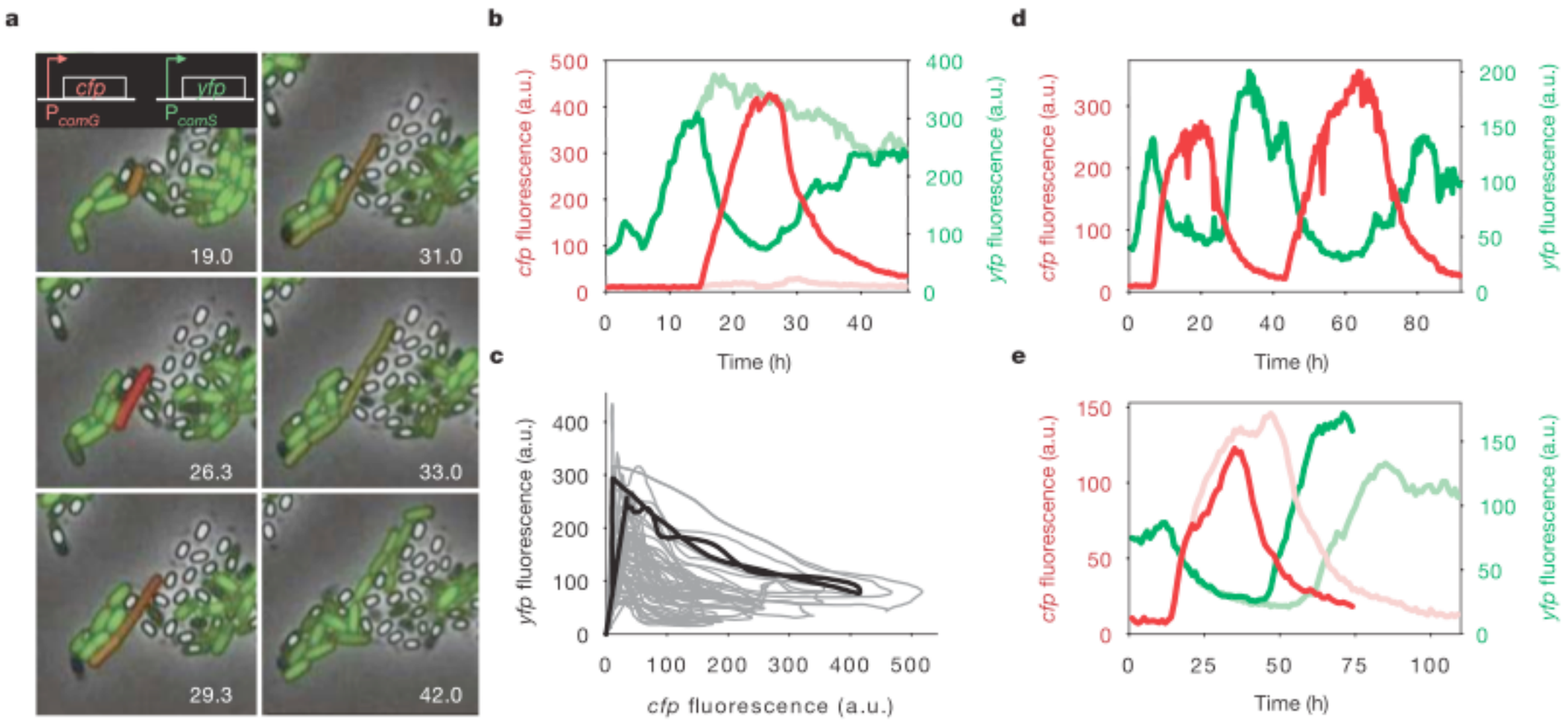
Excitable systems - competence

Gurol M. Suel, Jordi Garcia-Ojalvo, Louisa M. Liberman &
Michael B. Elowitz

An excitable gene regulatory circuit induces transient cellular differentiation

NATUREIVol 440I23 March 2006





Excitable systems - competence

$$\mathrm{MecA} + \mathrm{ComK} \overset{\gamma_{\pm a}}{\rightleftharpoons} \mathrm{MecA\text{-}ComK} \overset{\gamma_1}{\rightarrow} \mathrm{MecA}$$
$$\mathrm{MecA} + \mathrm{ComS} \overset{\gamma_{\pm b}}{\rightleftharpoons} \mathrm{MecA\text{-}ComS} \overset{\gamma_2}{\rightarrow} \mathrm{MecA}$$

$$\frac{dK}{dt} = \alpha_k + \frac{\beta_k K^n}{k_k^n + K^n} - \gamma_a M_f K + \gamma_{-a} M_K$$
$$\frac{dS}{dt} = \frac{\beta_s}{1 + (K/k_s)^p} - \gamma_b M_f S + \gamma_{-b} M_S$$
$$\frac{dM_K}{dt} = -(\gamma_{-a} + \gamma_1) M_K + \gamma_a M_f K$$
$$\frac{dM_S}{dt} = -(\gamma_{-b} + \gamma_2) M_K + \gamma_b M_f K$$

$$M_f + M_K + M_S = M_{\text{total}} = \text{constant}$$

$$\frac{dK}{dt} = a_k + \frac{b_k K^n}{k_0^n + K^n} - \frac{K}{1+K+S}$$
$$\frac{dS}{dt} = \frac{b_s}{1+(K/k_1)^p} - \frac{S}{1+K+S} + \xi(t)$$

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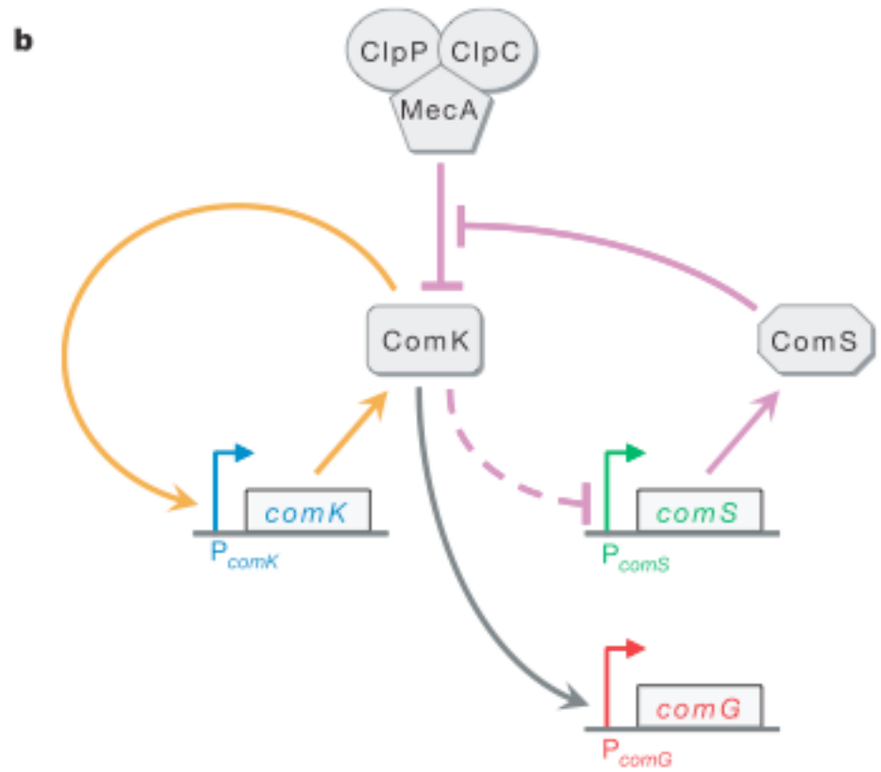
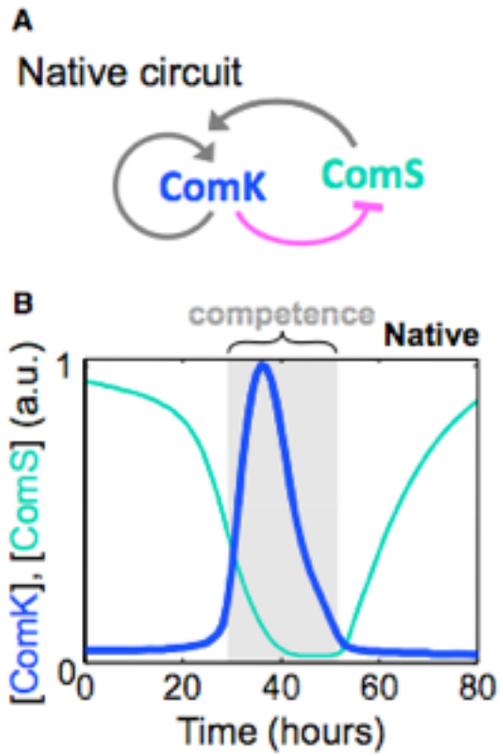
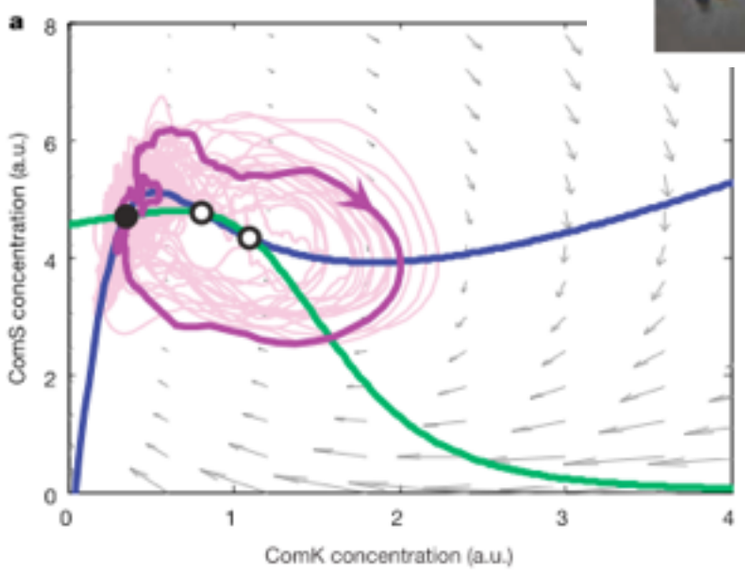
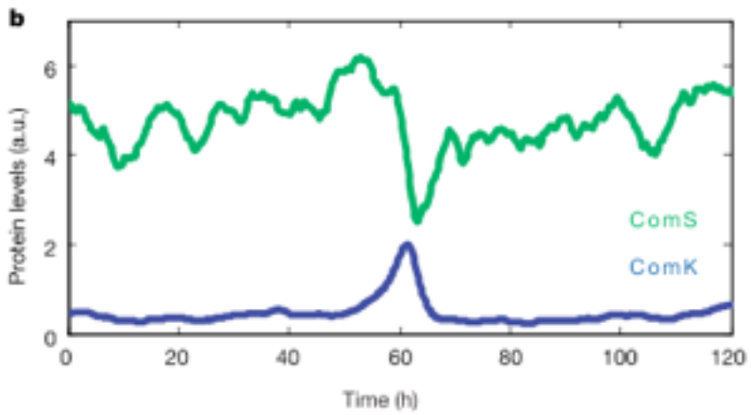
NATUREIVol 440I23 March 2006

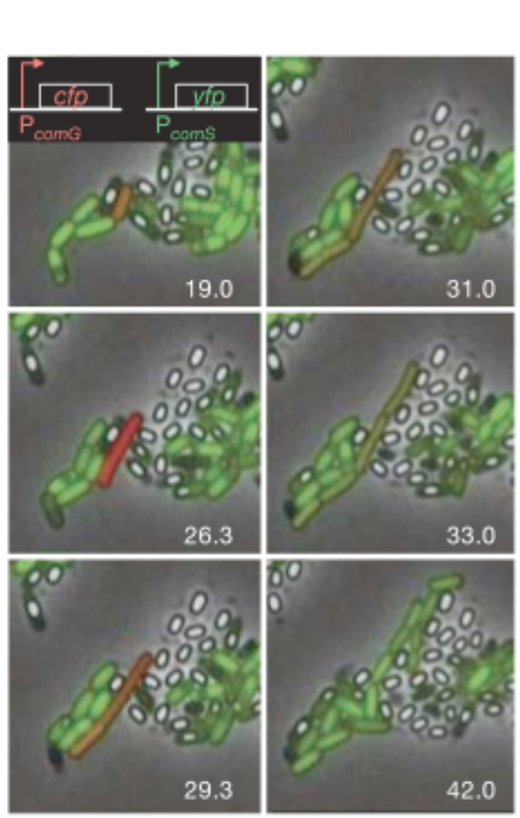


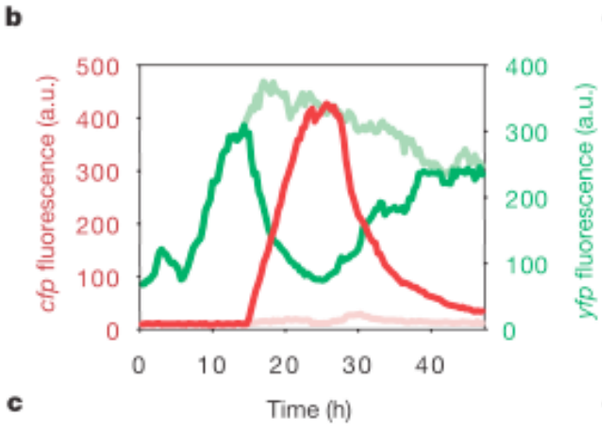


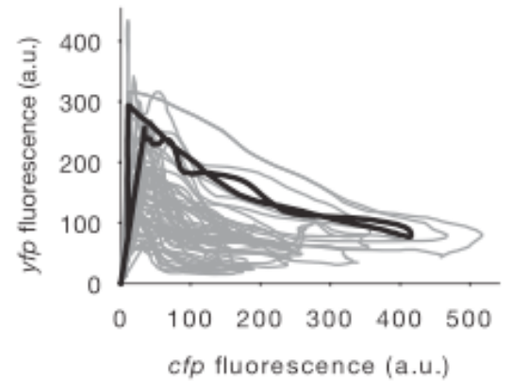
Excitable systems - competence

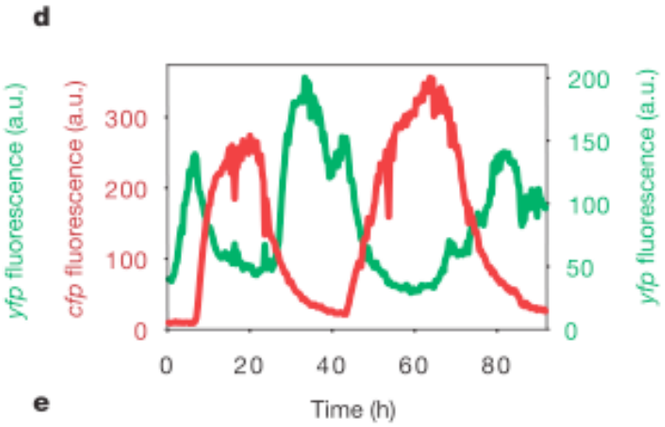


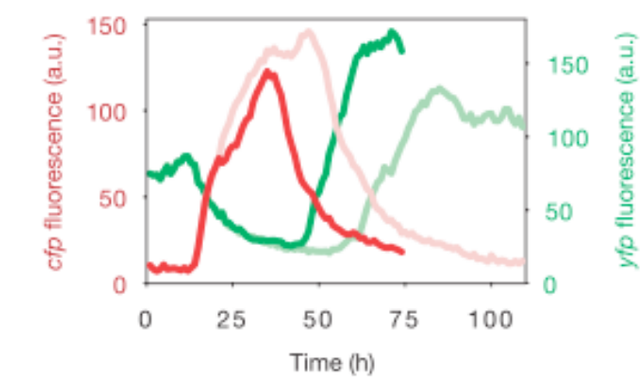












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$$\frac{dS}{dt} = \frac{b_s}{1+(K/k_1)^p} - \frac{S}{1+K+S} + \xi(t)$$

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Excitable systems - competence

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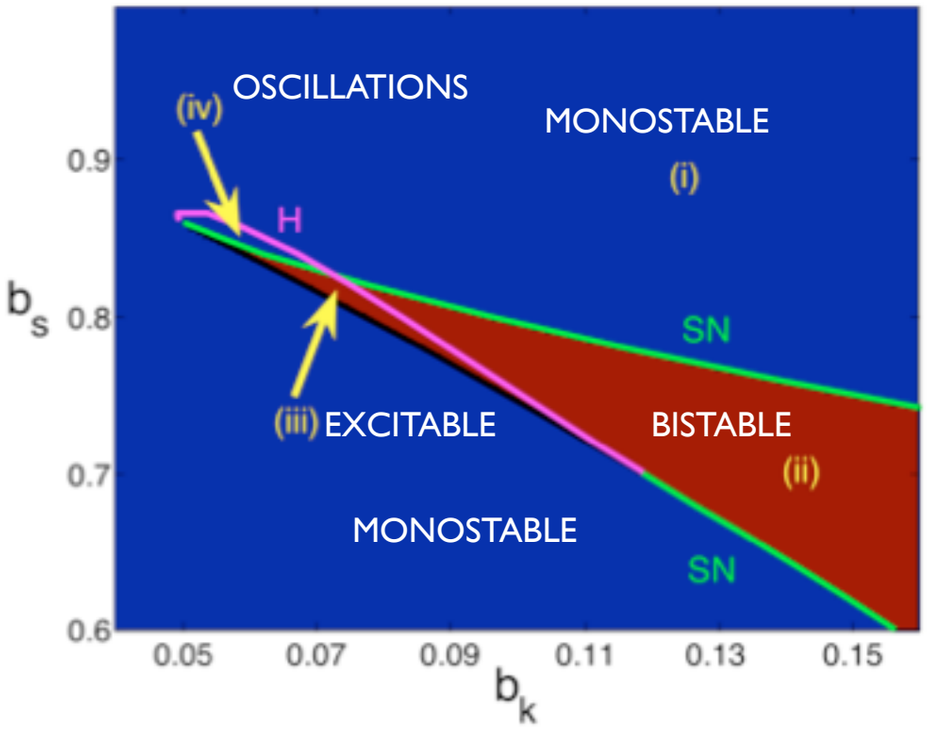

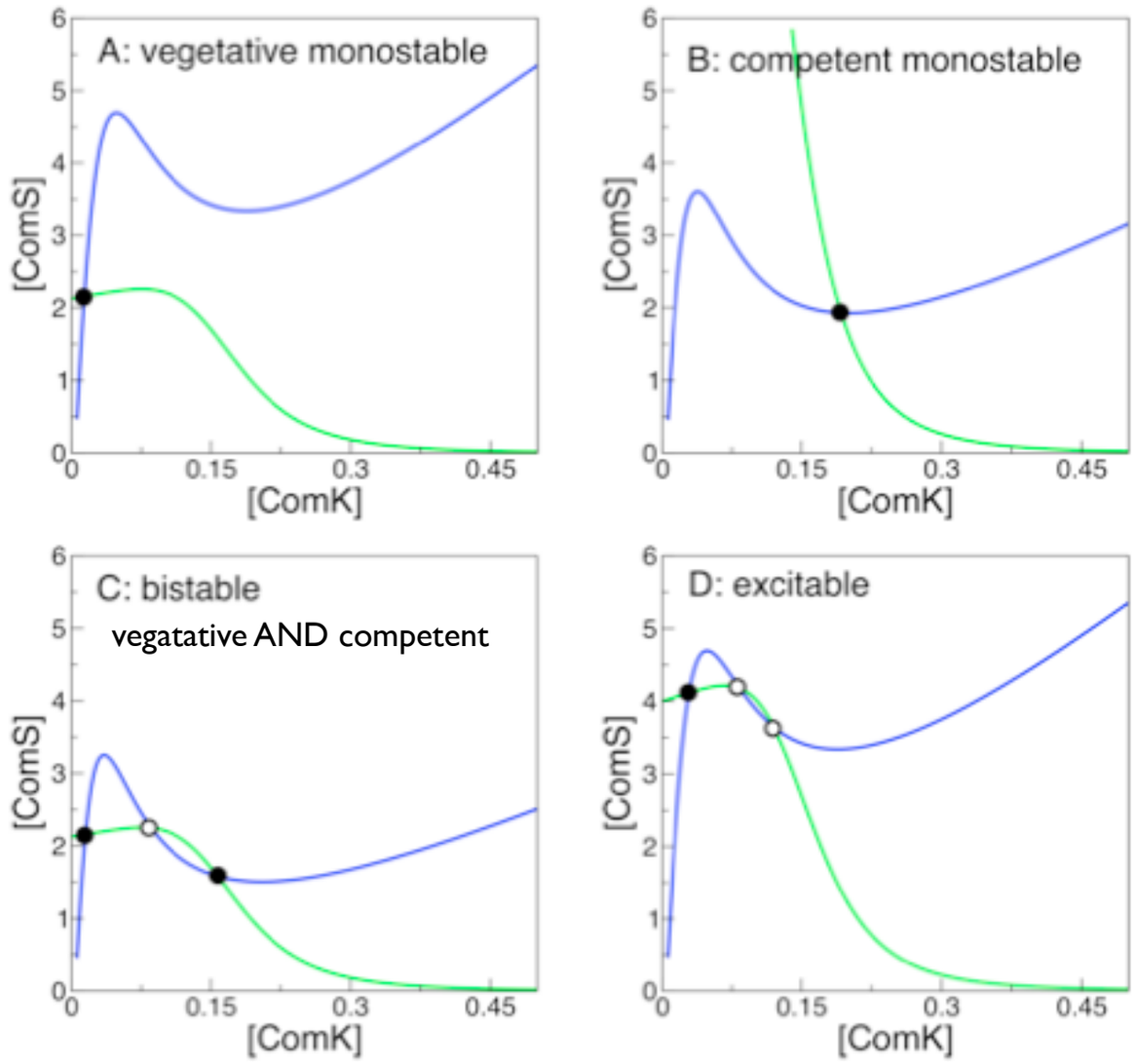

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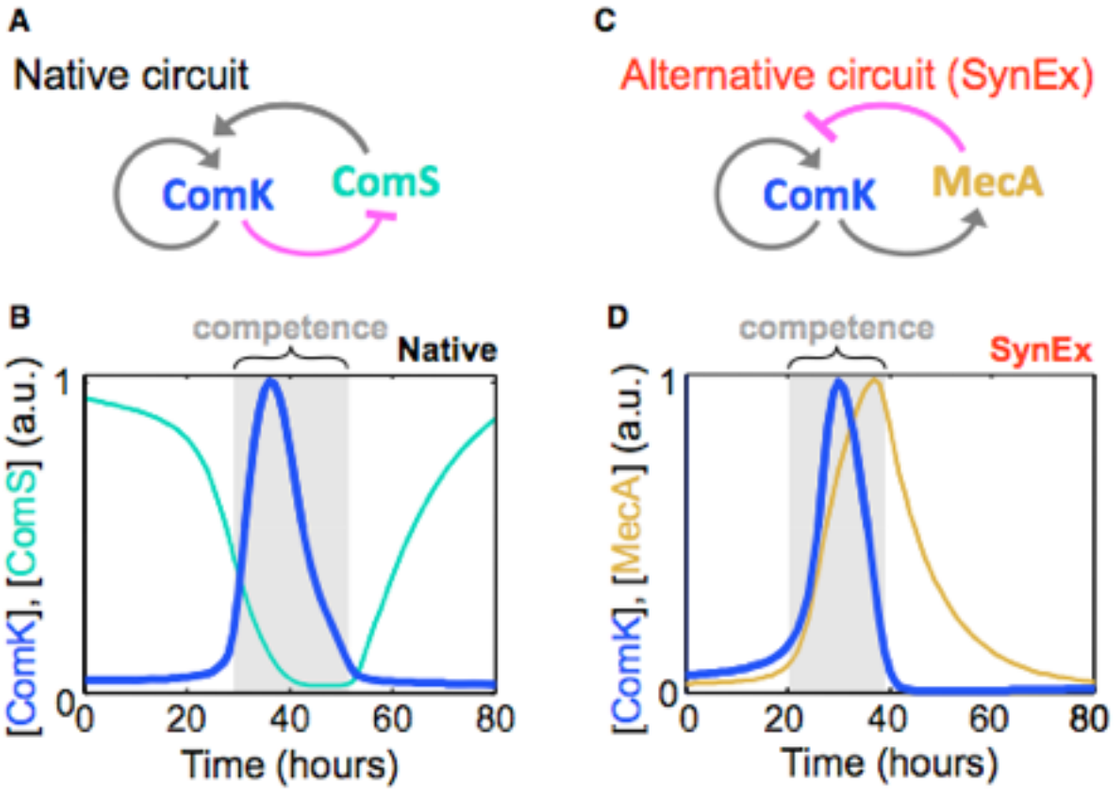
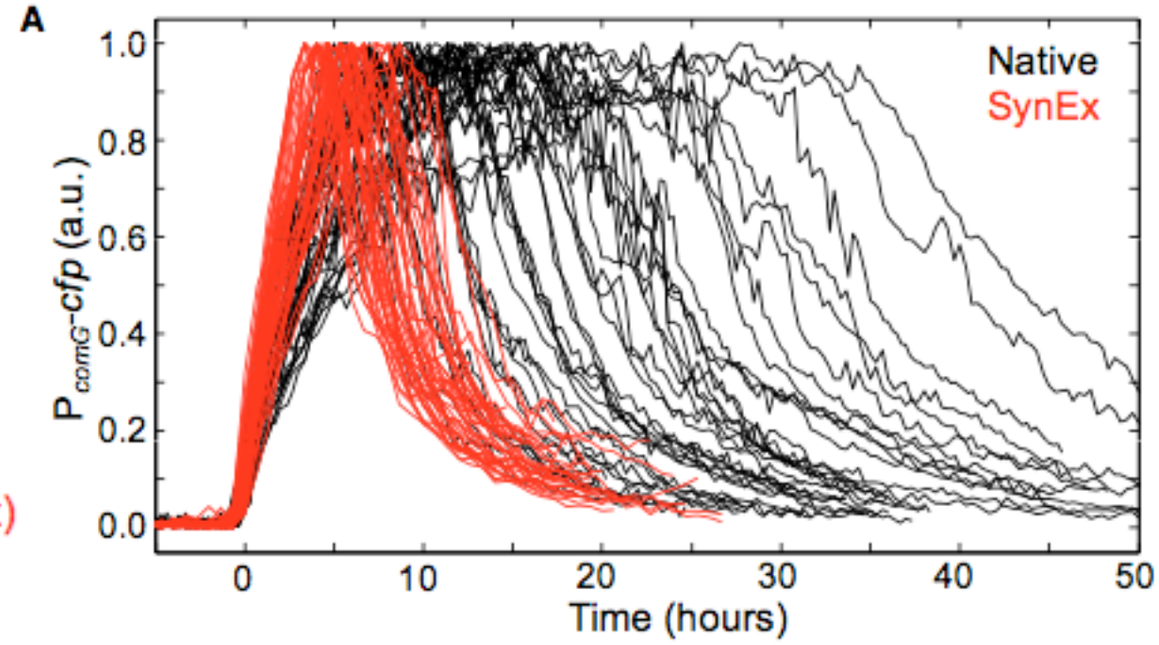
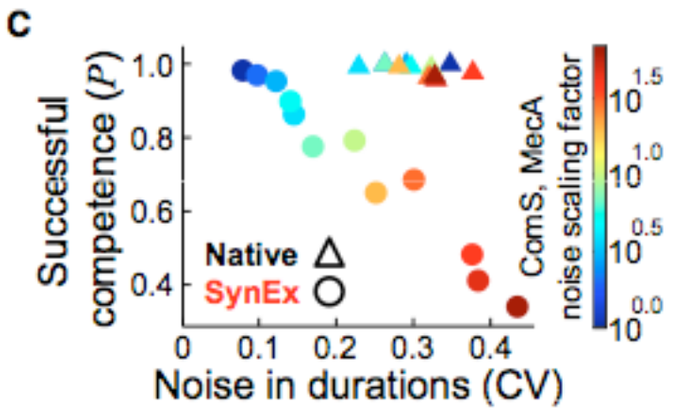
NATURE|Vol 440|23 March 2006

Competence - noise, form and function

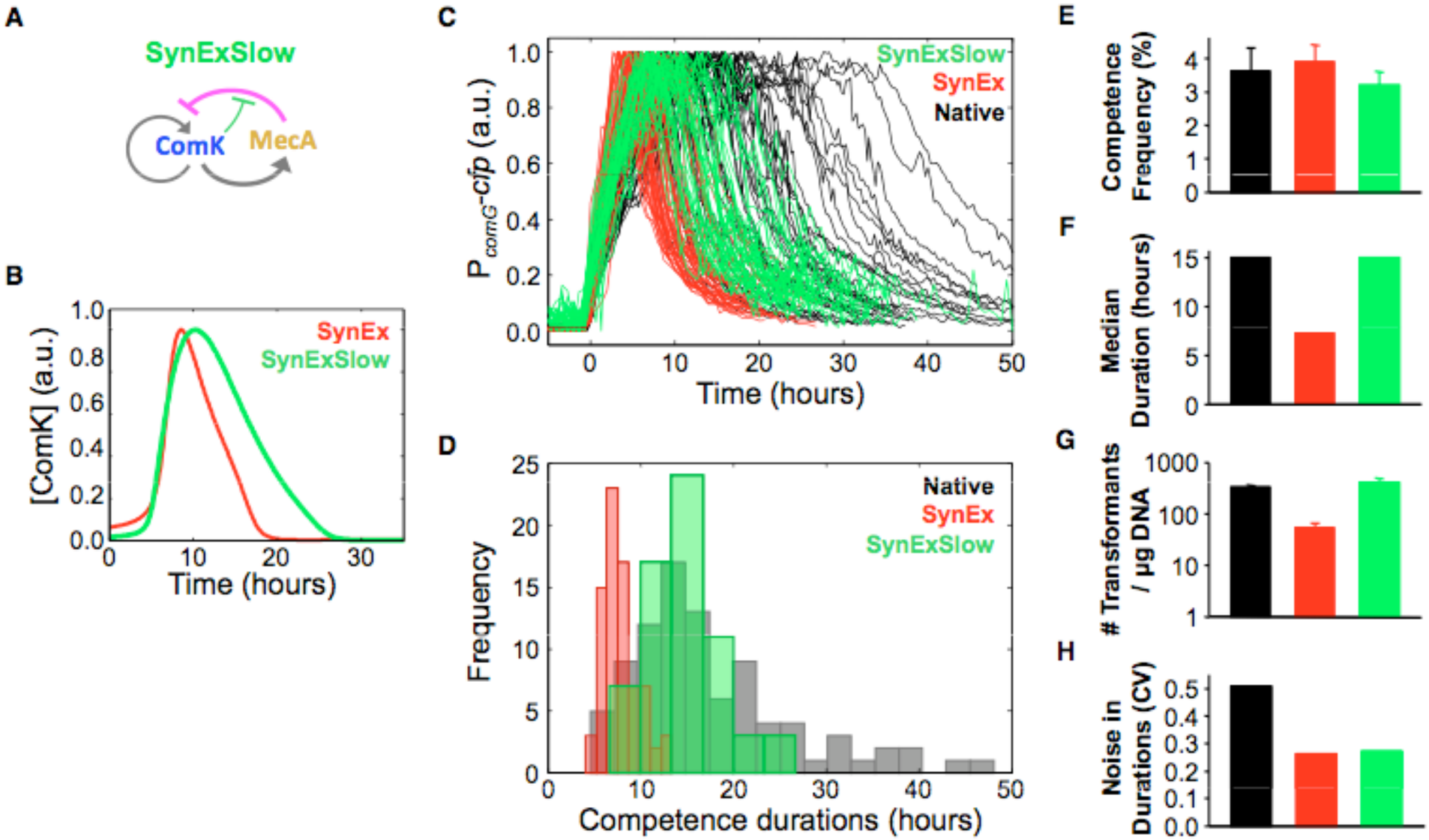






Tolga Cagatay, Marc Turcotte, Michael B. Elowitz,Jordi Garcia-Ojalvo,and Gurol M. Suel
Architecture-Dependent Noise Discriminates Functionally Analogous Differentiation Circuits
Cell 139, 1, 2009

Competence - noise, form and function



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