Biology of the *noisy* gene

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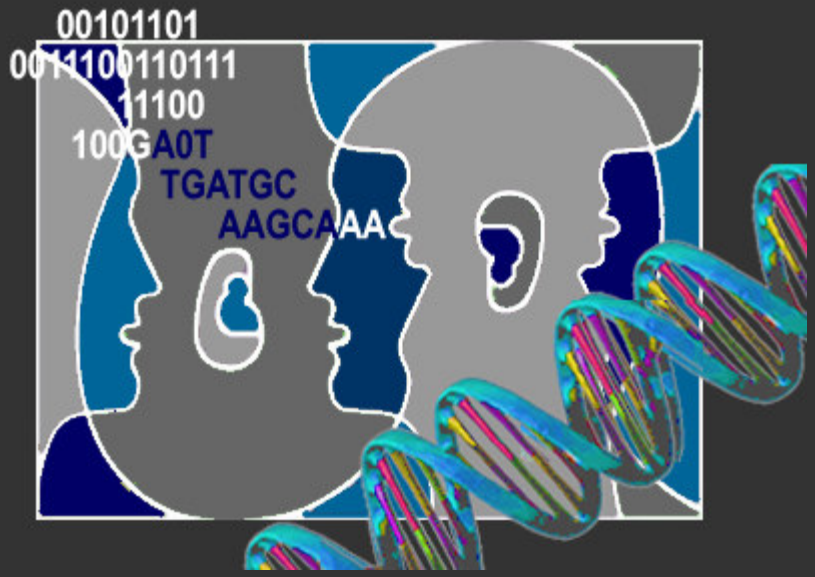
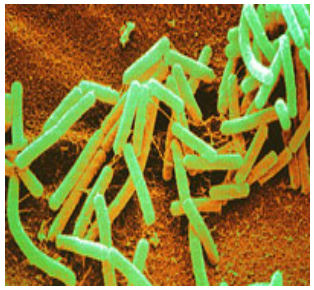
day IV: noisy eukaryotes
1) yeast



- Transcriptional and translational bursting.
- Gene activation.
- A more general model of gene expression noise.

Logs laboratory

Noisy prokaryotic genes

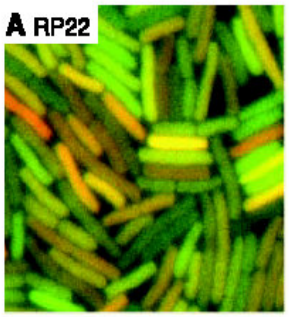


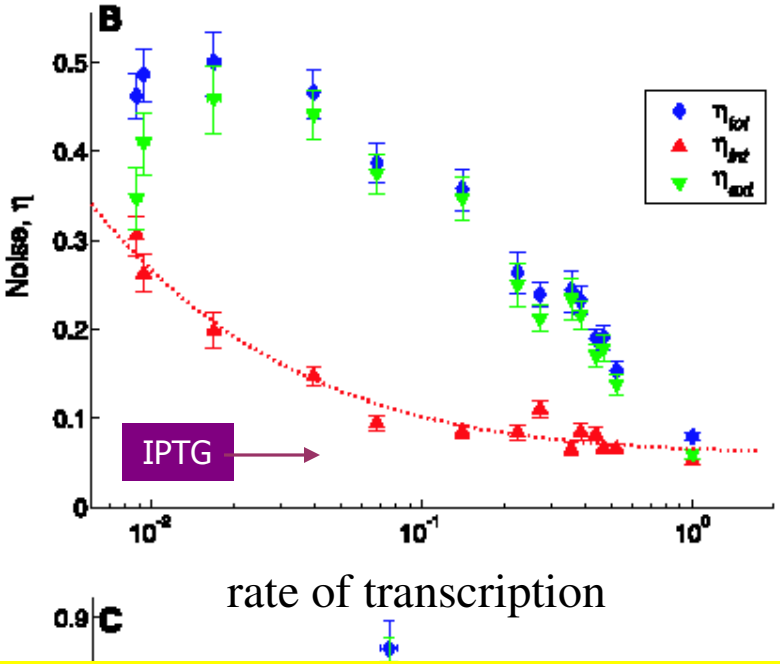
Noise associated to translational efficiency rather than transcriptional efficiency (translational bursting)

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

Inefficient translation → Less noise

Noisy prokaryotic genes



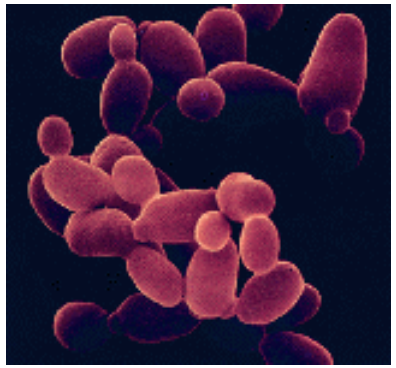


Other sources of variability (external to gene expression): external noise

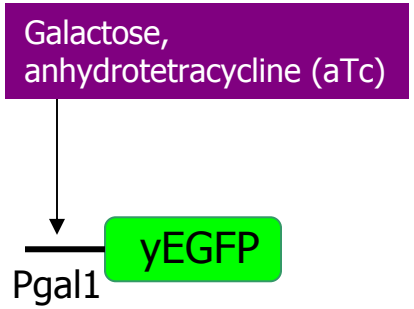
Two reporter strategy: Two (almost) identical fluorescence proteins
Simultaneously expressed from same promoters.

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

Noisy eukaryotic genes



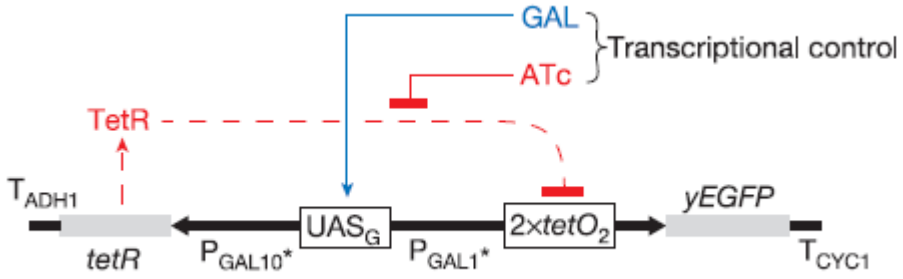
yeast



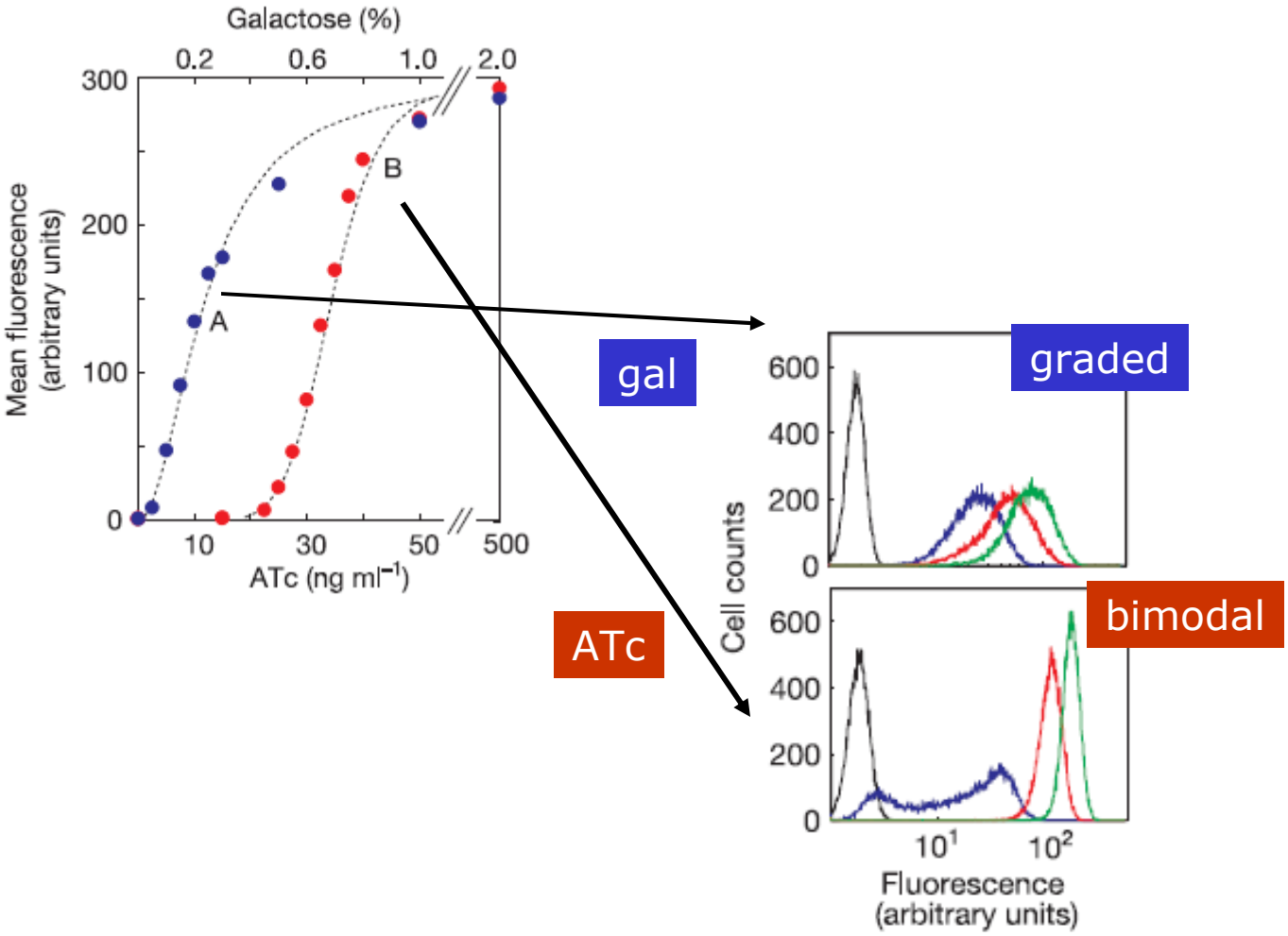
Several strategies to modify transcription and translation efficienty

- Native; galactose
- Artificial; Tet-responsive

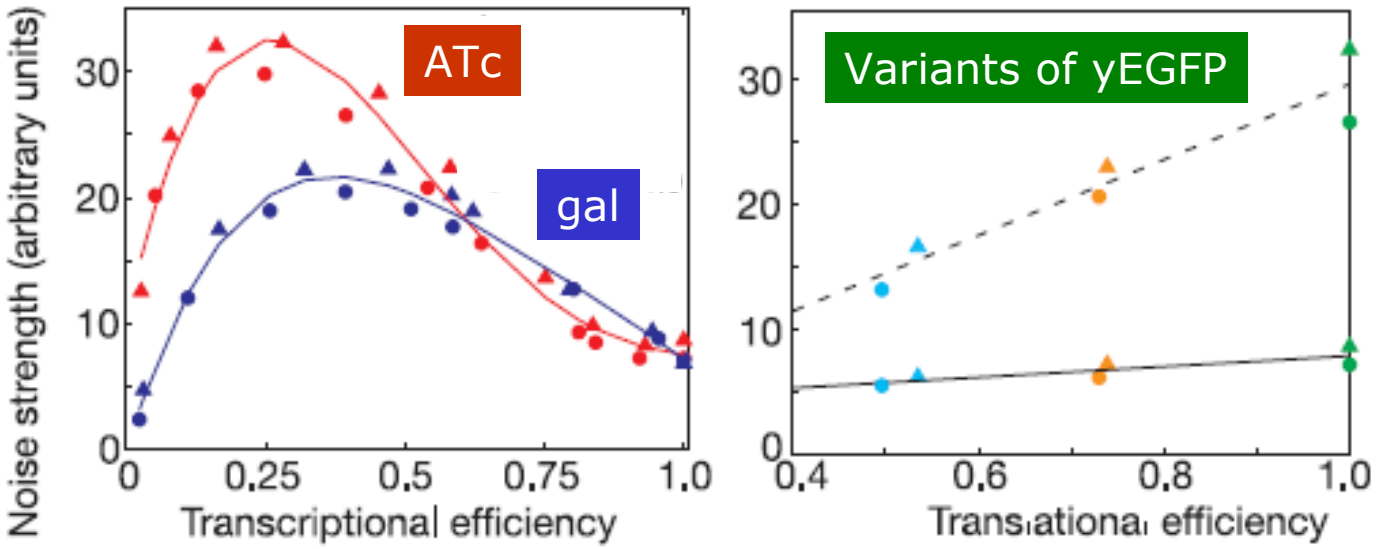
- yEGFP; yeast-enhanced GFP



Comparison galactose *vs.* ATc-mediated induction



Transcriptional bursting

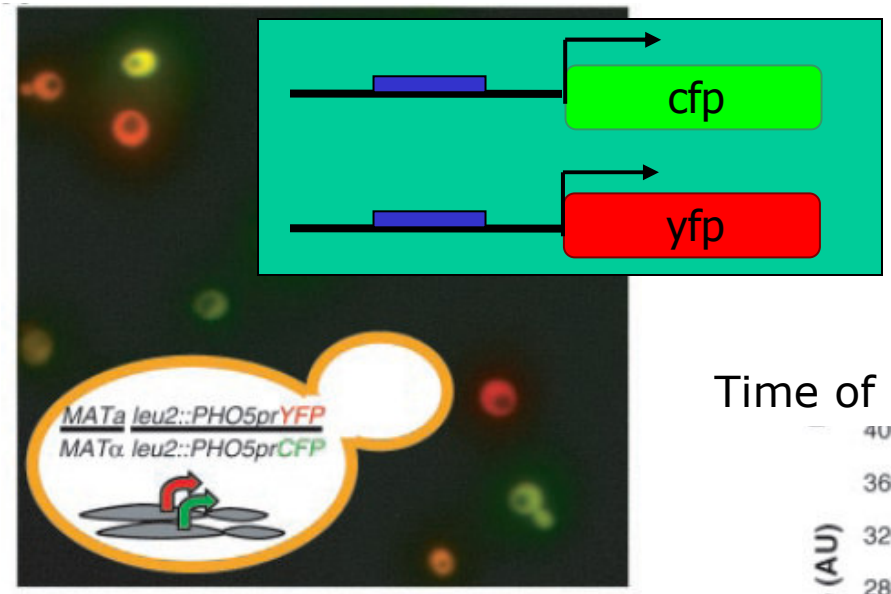


Main conclusions:

- translational bursting as in prokaryotes

- transcriptional bursting: slow transitions between promoters states: chromating remodelling, etc.

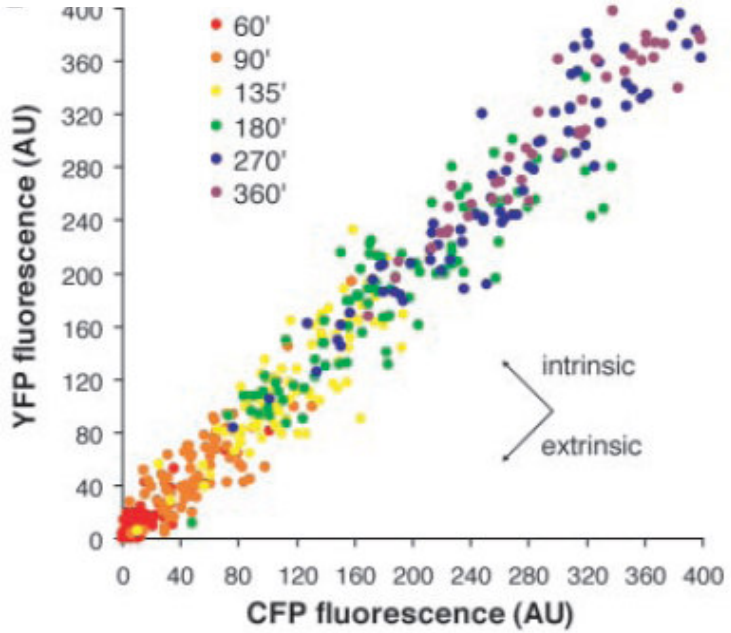
Intrinsic/extrinsic gene noise



Dual reporter technique;

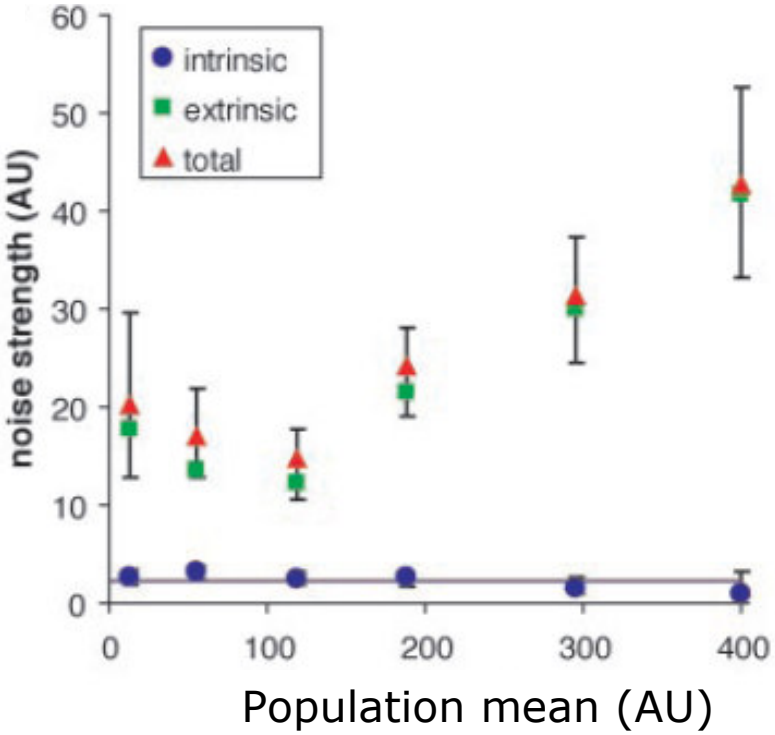
Pho5pr induction
by phosphatase starvation

Time of induction



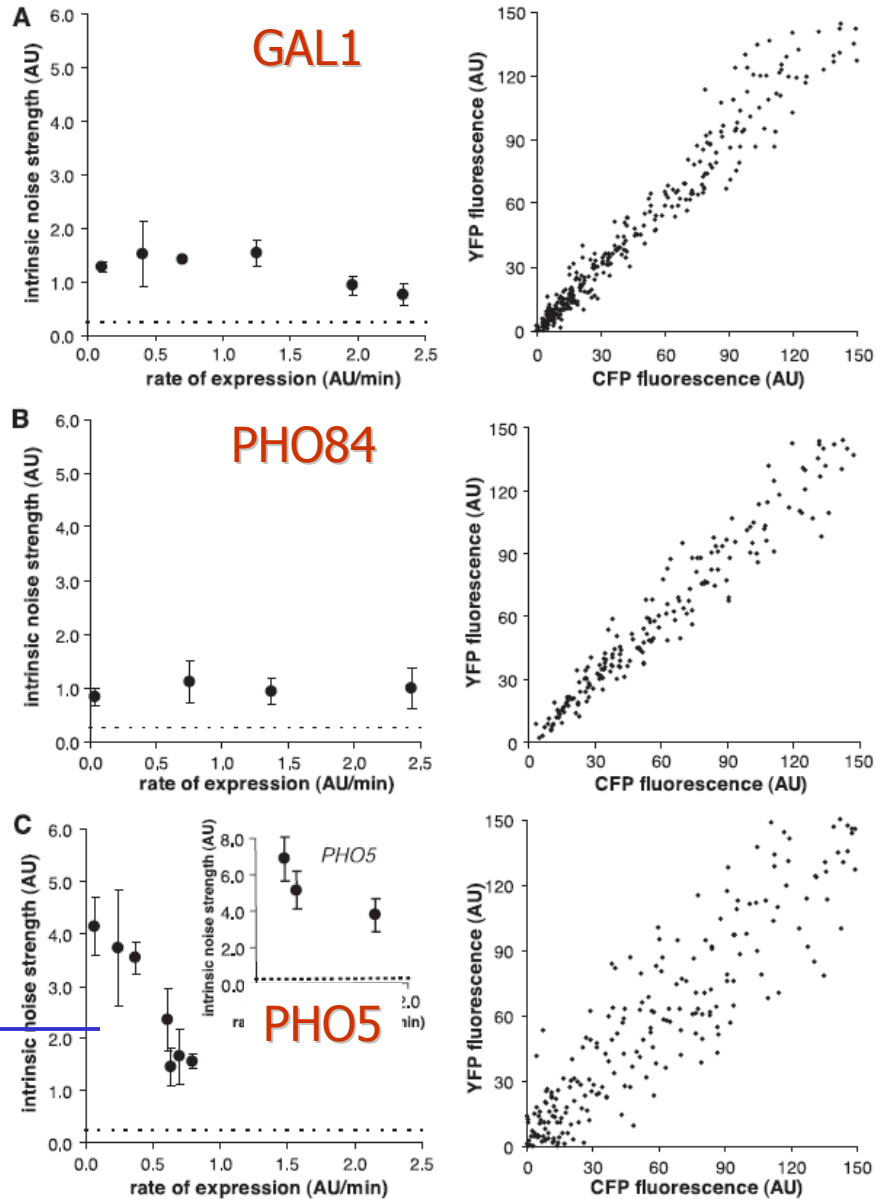
Extrinsic factors dominates gene noise

From now on → Noise strength: = Fano (variance/mean)



Intrinsic noise is promoter-specific

Different promoters induced with different galactose concentrations.

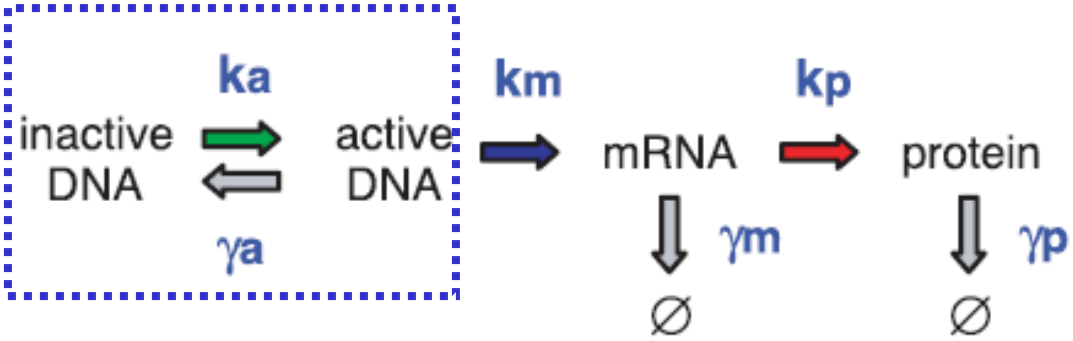


Maximal induction

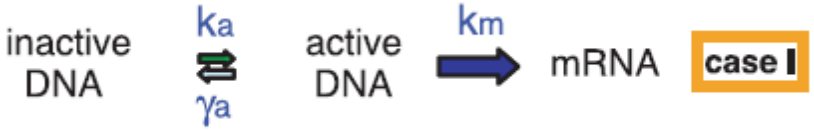
Different to previous models!

But … Pho5 follows a promoter Transition step.

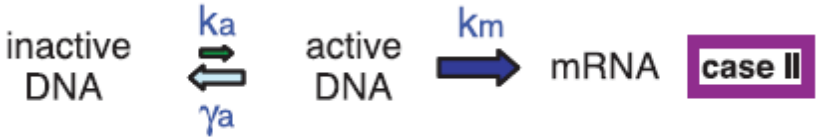
Different models



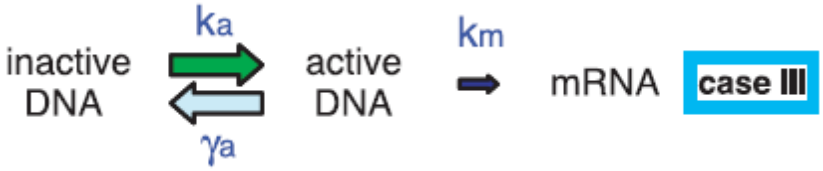
E.g.,
Case I; slow chromating remodelling



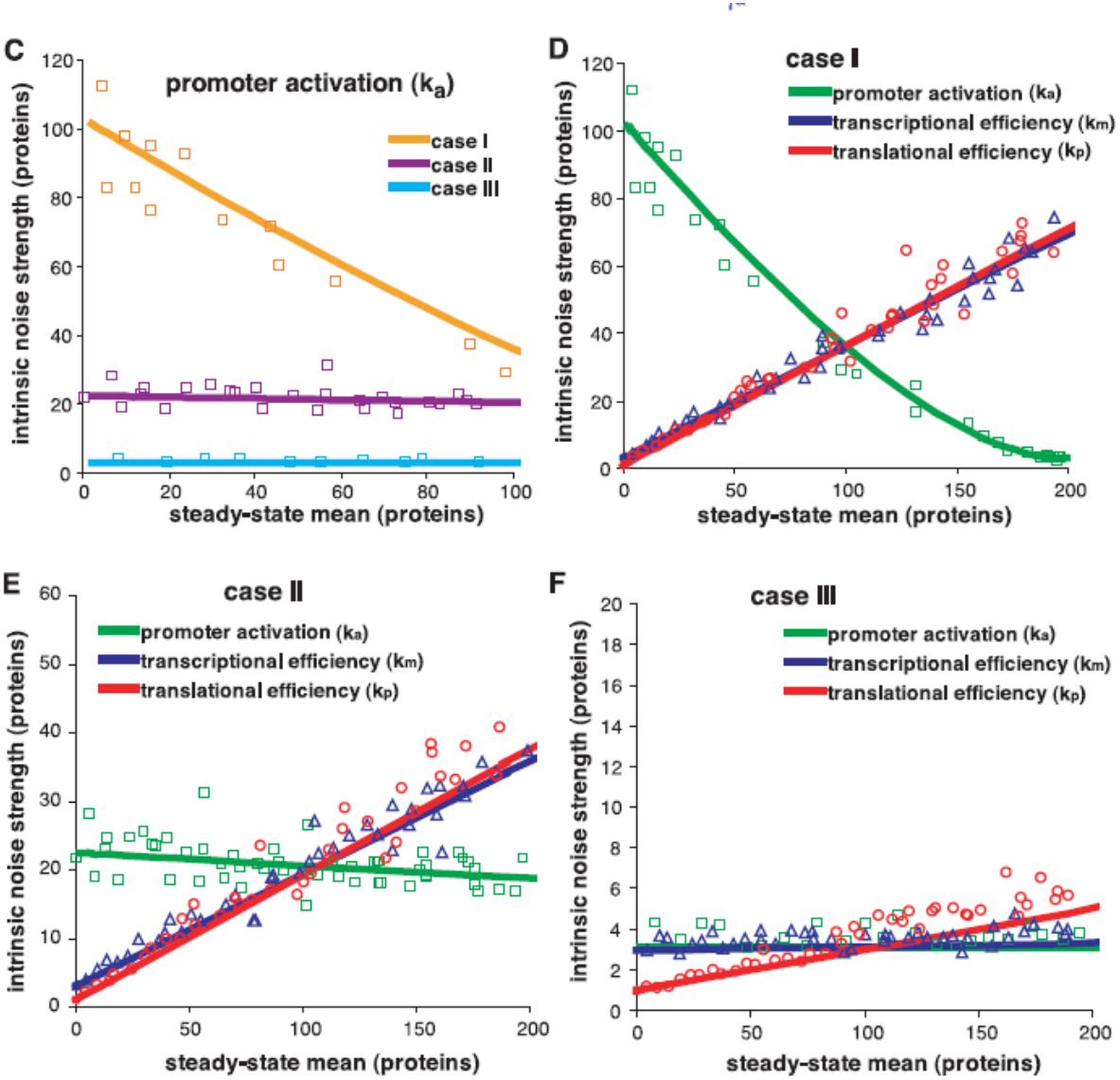
Case II; nucleosome sliding or
Prokaryotic DNA looping



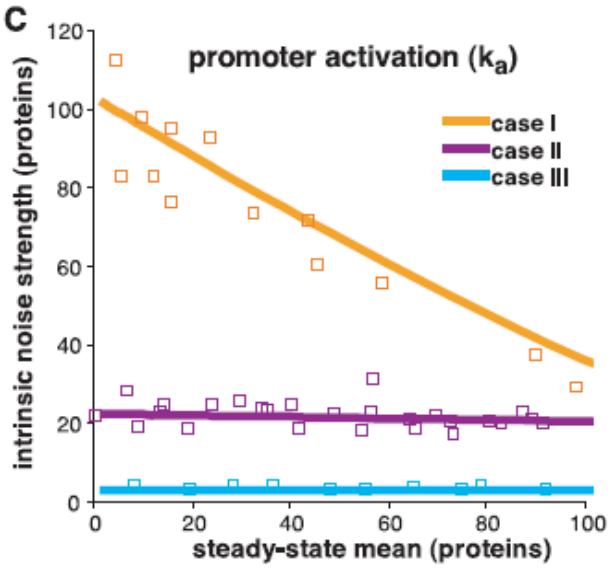
Case III; rapid binding/unbinding
as in prokaryotes

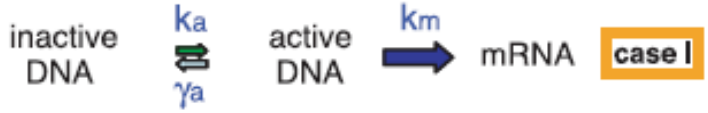


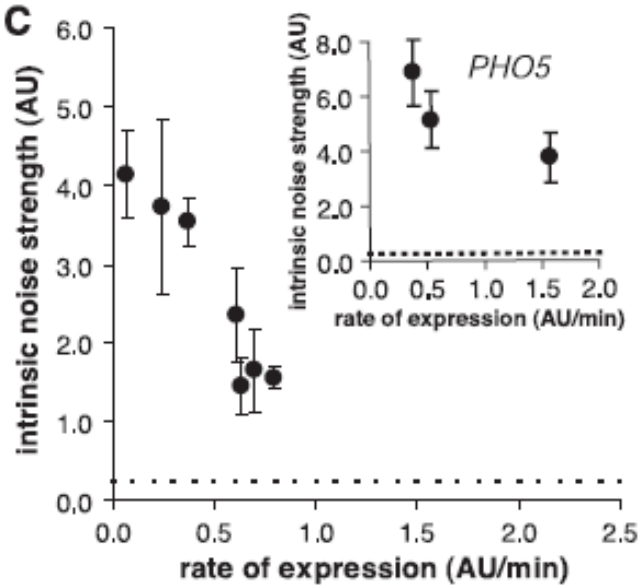
Different models; predictions



Different models; predictions + experiments







Confirming experiments

Lacking remodelling constituents

Modified chromating remodeling

Decreasing noise with decreasing rate of gene expression