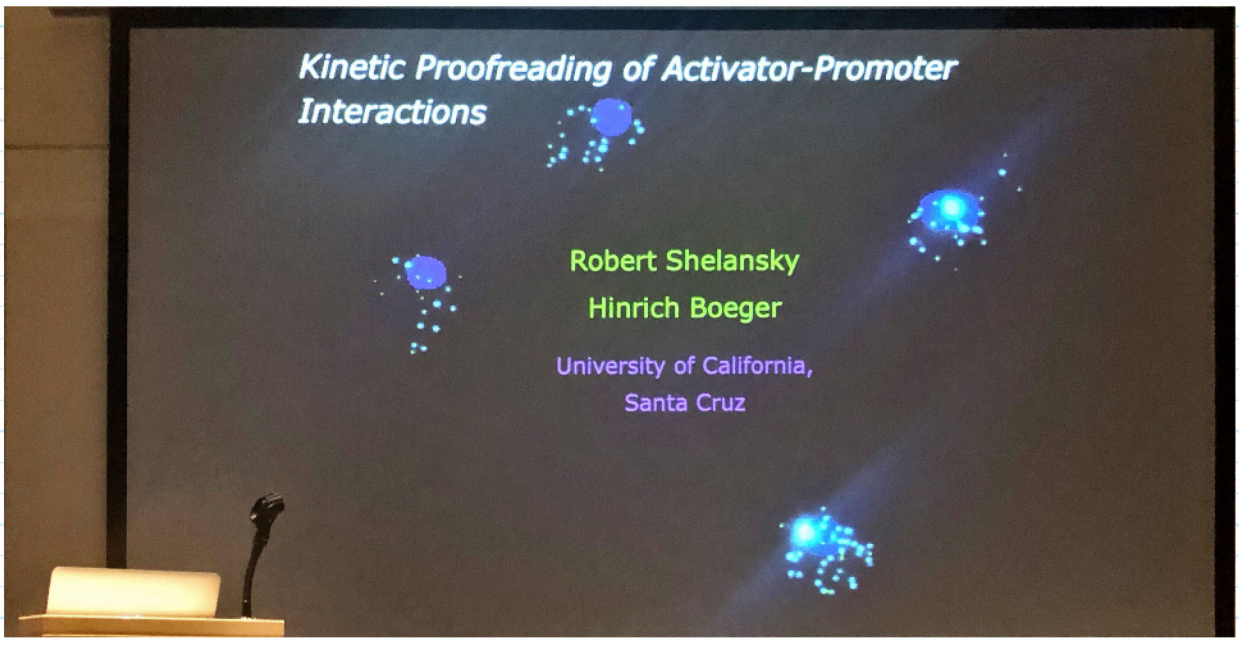
$$\frac{\sigma^2}{\langle m^1 \rangle} = 1 + \langle m^1 \rangle \frac{k^-}{k^+} \frac{\gamma}{k^+ + k^- + \gamma}.$$

$$= 1 + \frac{r}{\gamma} \frac{k_{off}}{k_{on}} \frac{\gamma}{k_{off} + k_{on} + \gamma}$$

Hinrich Boeger



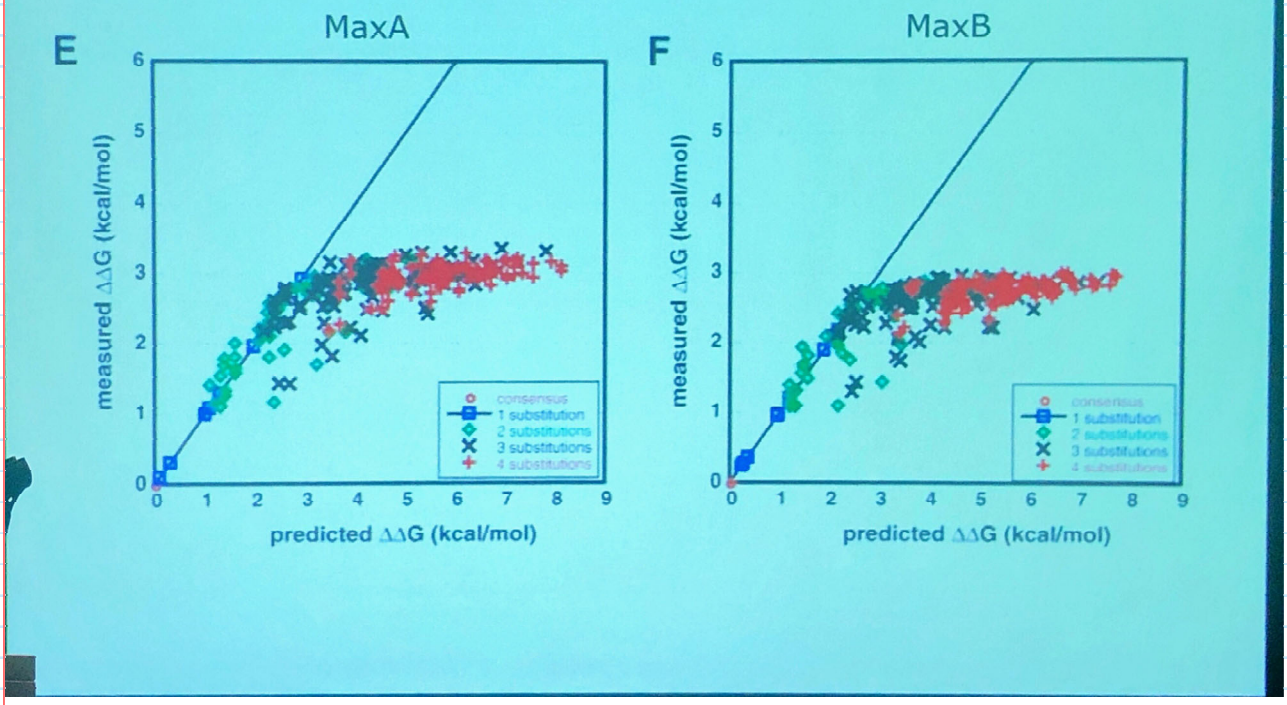
↳ Binding of correct and

incorrect activator to o. promoter

Energetics of Activator-DNA Binding

(Maerkl and Quake, 2007)

$$\Delta\Delta G^{\circ} = RT \ln f_0$$



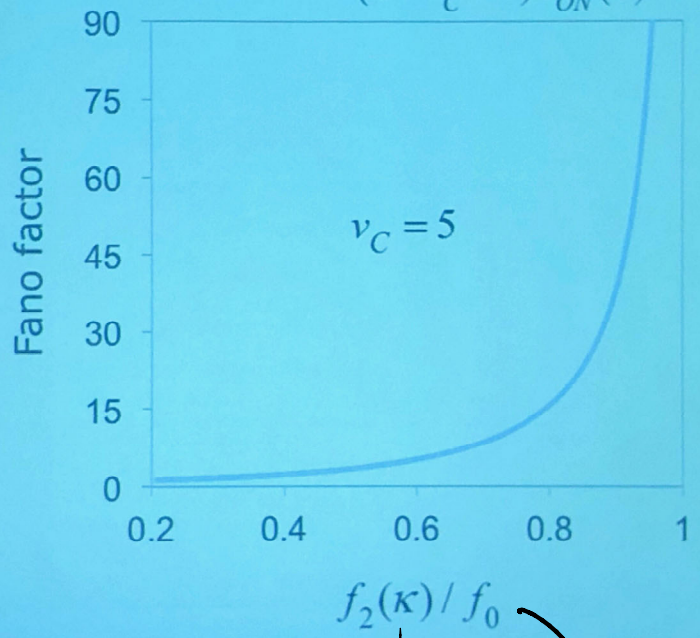
$\Rightarrow f_0 \simeq 100$

$(\omega / k_{on} \to 0)$ → in the context of a 2-state model

model

Noise Catastrophe

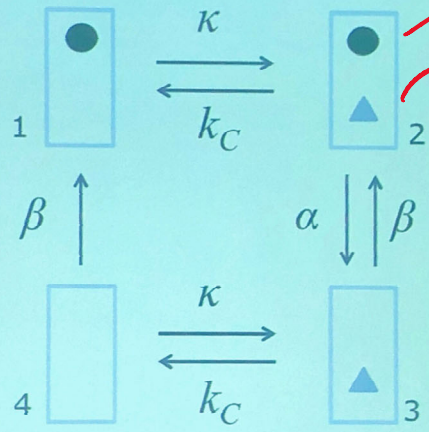
$$\mathbb{F}_R(\kappa) = 1 + \frac{[1-\pi_{ON}(\kappa)]\nu_C}{(\kappa + k_C + \delta)\pi_{ON}(\kappa)}$$



k_{on}

thermodynamic limit

Four-State Promoter Model



nucleosome

activator

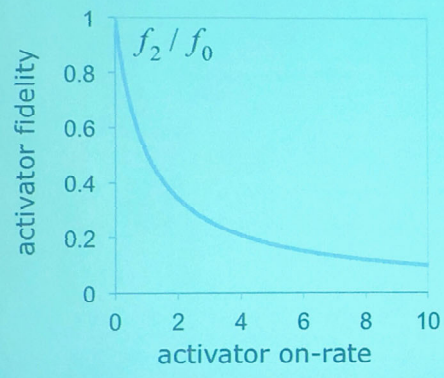
nucleosome can only be removed by activator

transcription

Kinetic Proofreading Allows for Activator Fidelities Beyond f_0

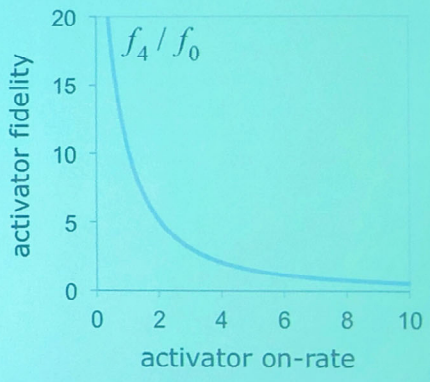
Two-state

$\max f_2 = f_0$

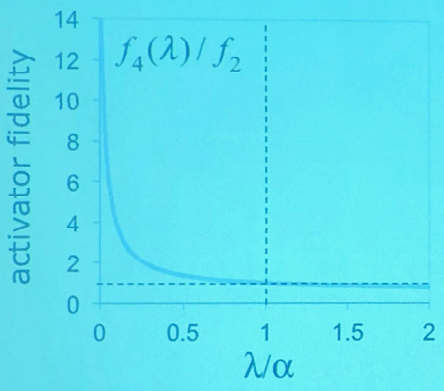


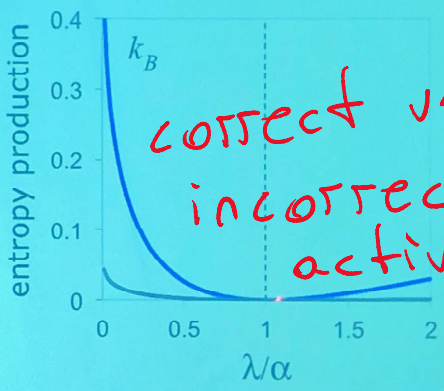
Four-state

$\max f_4 = f_0^2$



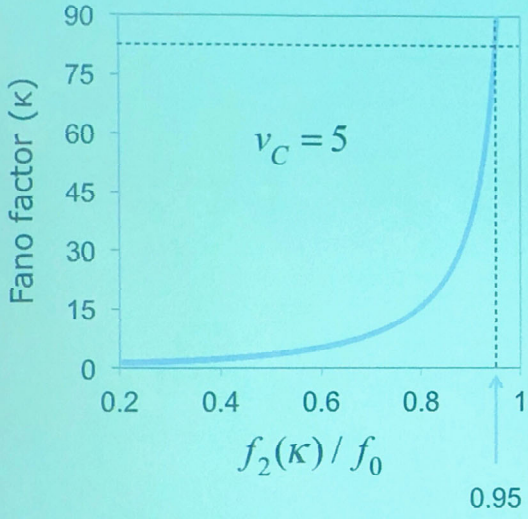
Kinetic Proofreading Requires Entropy Production

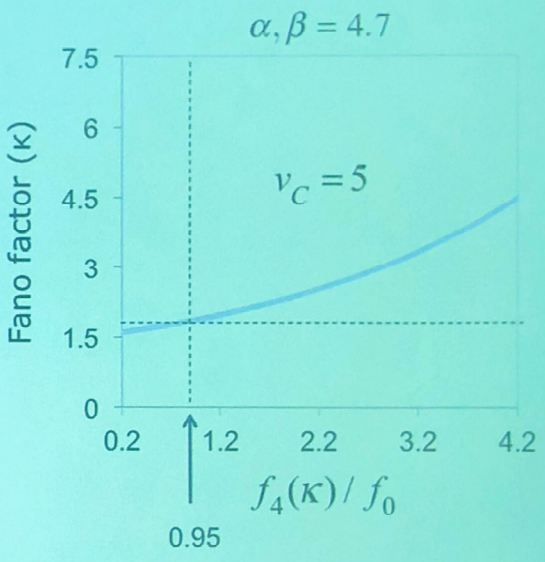




correct vs. incorrect activator binding

Kinetic Proofreading Avoids Noise Catastrophe





Examples: Sample Paths

$f / f_0 = 0.95$