Stochastic Phenomena in Biological Systems

Kyung H. Kim

Stochastic Phenomena

- Stochastic Focusing
- Stochastic Switching
- Single Events
- Multiplicative Noise Effect

Stochastic Gene Regulatory Network

- Stochastic Focusing
- Stochastic Switching
- Single Events
- Multiplicative Noise Effect

Stochastic Focusing

- Stochastic Focusing:

  Sensitivity increase due to stochastic effects.

- Sensitivity:

$$\text{Sensitivity} = \frac{\%\ \text{Change of Response Signal}}{\%\ \text{Change of Source Signal}}$$

The sensitivity can be used to estimate how a system responds due to changes in the environment.

$$\text{Sensitivity} = \frac{dX}{dY}\frac{Y}{X} = \frac{d\ln X}{d\ln Y}.$$

where we used $\dfrac{d\ln f(x)}{dx} = \dfrac{1}{f(x)}\dfrac{df(x)}{dx}$, $d\ln f(x) = \dfrac{1}{f(x)}df(x).$

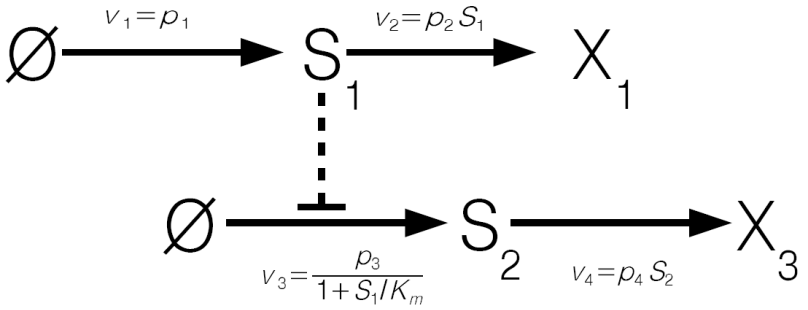
Stochastic Focusing

- Stochastic Focusing:

  Sensitivity increase due to stochastic effects.

  [Paulsson, et al. PNAS 97, 7148-7153 (2000)]

  Two step cascade reactions



Source Signal = S1

Response Signal = S2

$$\text{Sensitivity} = \frac{d\langle S_2\rangle}{d\langle S_1\rangle}\frac{\langle S_1\rangle}{\langle S_2\rangle} = \frac{d\ln\langle S_2\rangle}{d\ln\langle S_1\rangle}$$

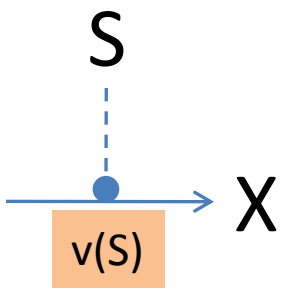
$$\langle x\rangle = Mean(x)$$

Stochastic Focusing

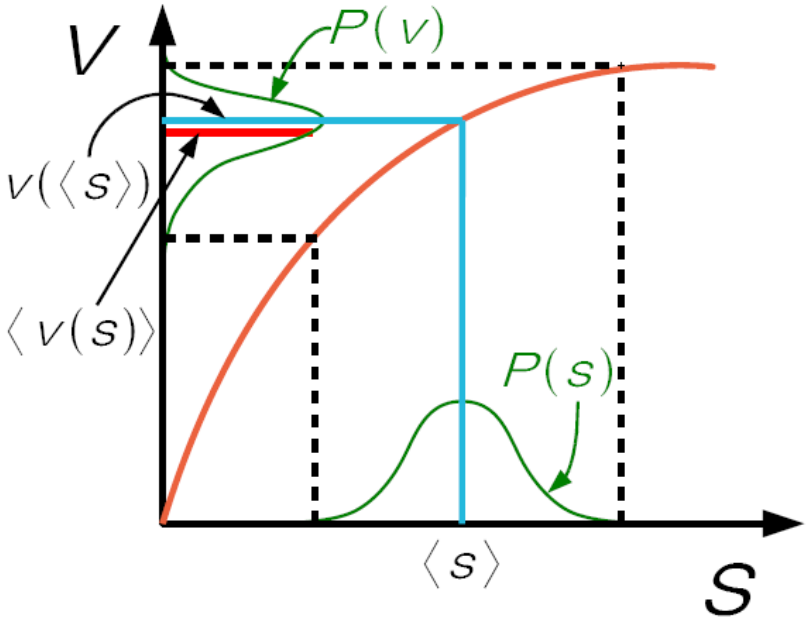
Fluctuations in the concentration of S leads to fluctuations in the reaction rate v(S).

How does the mean rate of reaction change with the noise?

E.g.,



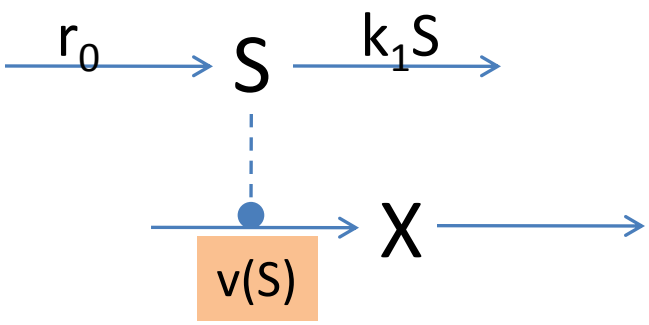
$$v(S) = \frac{k_2 S}{K_M + S}$$

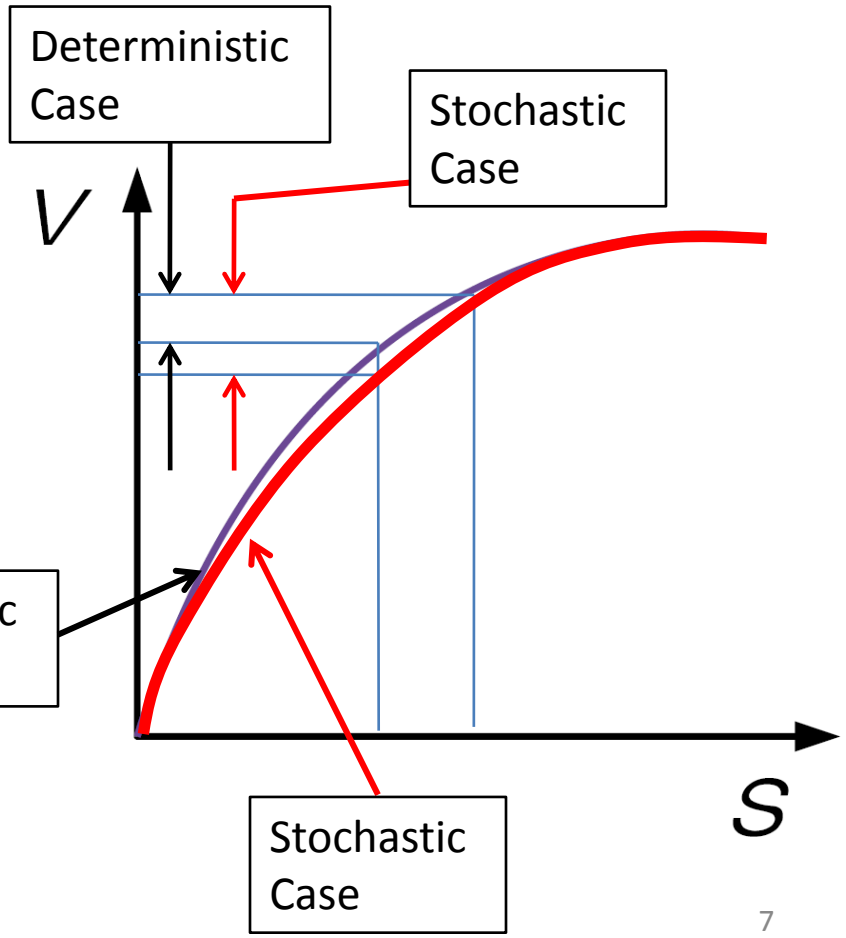


Stochastic Focusing

- We can change mean S by changing r_0.
- The change of mean rate increases with stochastic noise.
- Sensitivity increases.

  → "Stochastic Focusing".

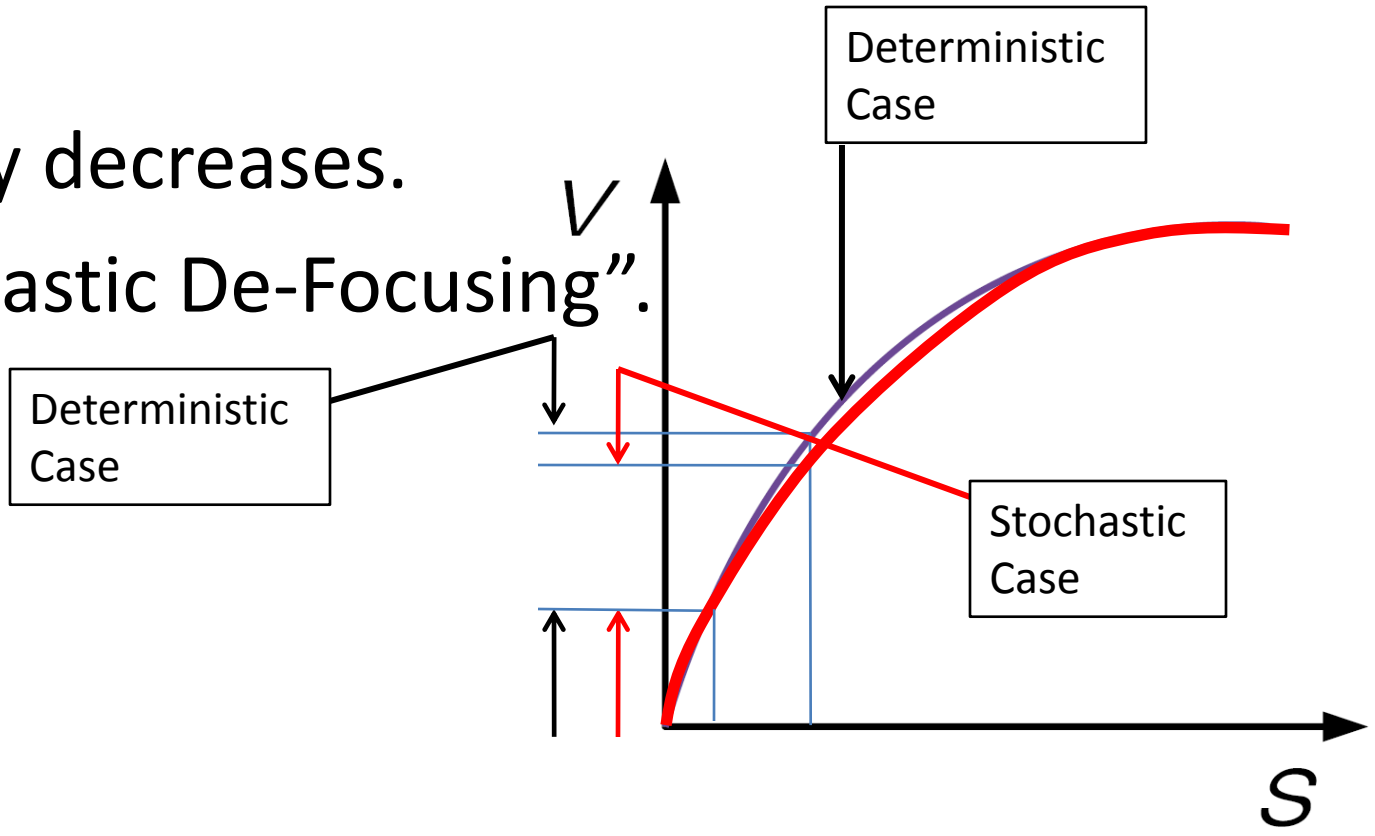




Stochastic De-Focusing

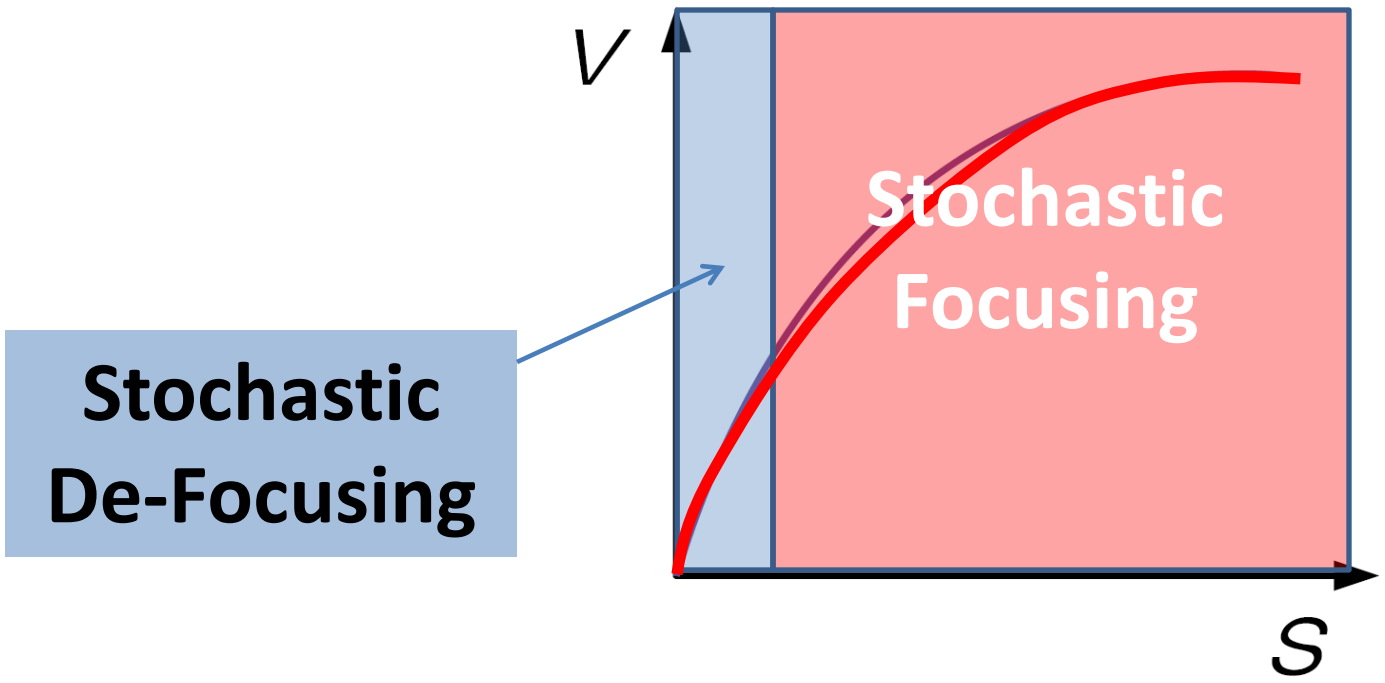
- The change of v decreases with stochastic noise.
- Sensitivity decreases.

  → “Stochastic De-Focusing”.



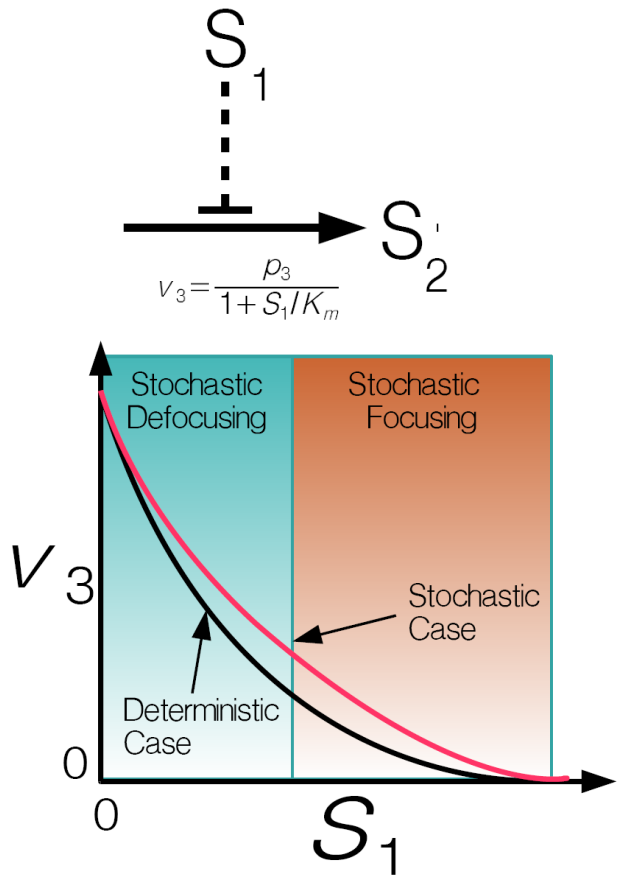
Stochastic Focusing-Defocusing Compensation

- Stochastic focusing can occur in one region of the curve and stochastic defocusing in another region.

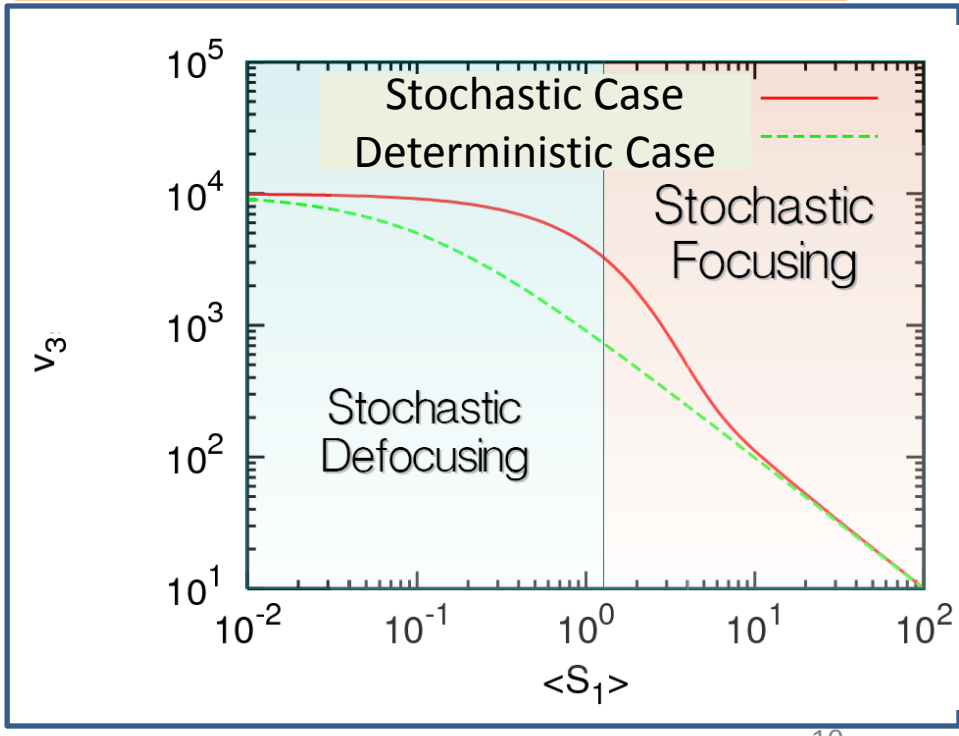


Stochastic Focusing

Two step cascade reactions [Paulsson, et al. PNAS 97, 7148 (2000)]

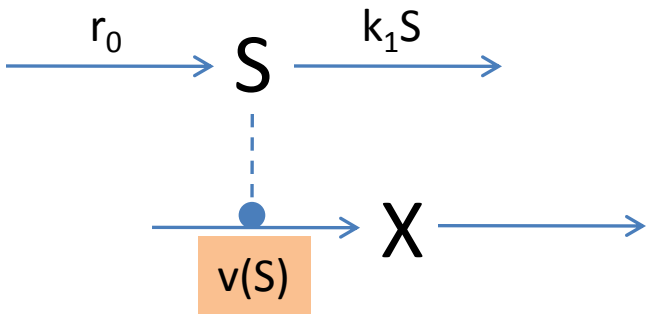


$$\text{Sensitivity} = \frac{d\langle v_3\rangle}{d\langle S_1\rangle}\frac{\langle S_1\rangle}{\langle v_3\rangle} = \frac{d\ln\langle v_3\rangle}{d\ln\langle S_1\rangle}.$$



Stochastic Focusing

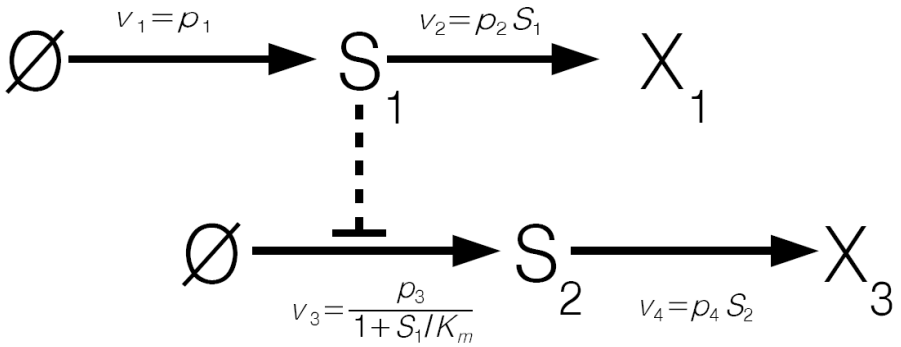
Consider these effects in a pathway such as the one below.



$$v(S) = \frac{k_2 S}{K_M + S}$$

Stochastic Focusing

Two step cascade reactions [Paulsson, et al. PNAS 97, 7148 (2000)]



$$\text{Sensitivity} = \frac{d\langle v_3\rangle}{d\langle S_1\rangle}\frac{\langle S_1\rangle}{\langle v_3\rangle} = \frac{d\ln\langle v_3\rangle}{d\ln\langle S_1\rangle}.$$

$$Mean(v_3) = p_4 Mean(S_2).$$

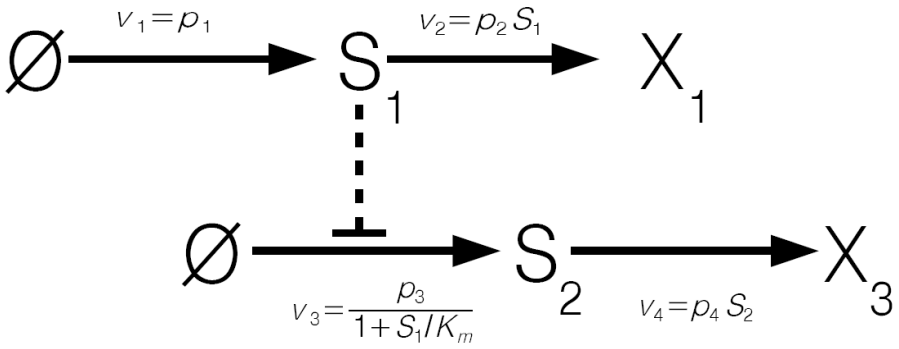
$$Mean(S_2) = \frac{Mean(v_3)}{p_4}.$$

$$\ln[Mean(S_2)] = \ln[Mean(v_3)] - \ln[p_4].$$

$$d\ln[Mean(S_2)] = d\ln[Mean(v_3)] - d\ln[p_4].$$

Stochastic Focusing

Two step cascade reactions [Paulsson, et al. PNAS 97, 7148 (2000)]



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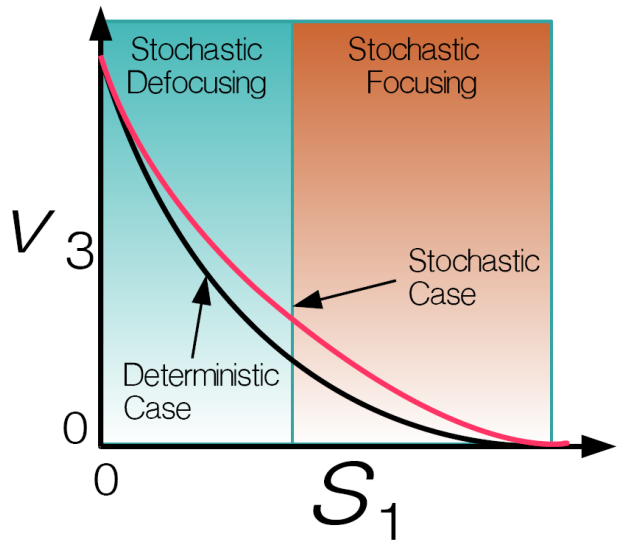

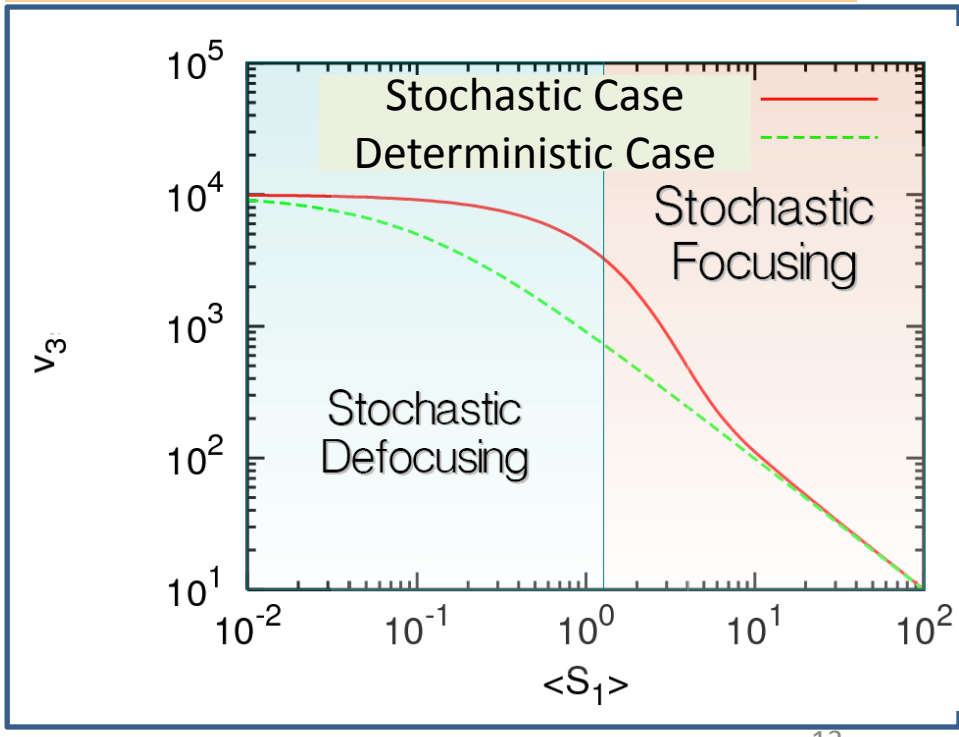

Stochastic Gene Regulatory Network

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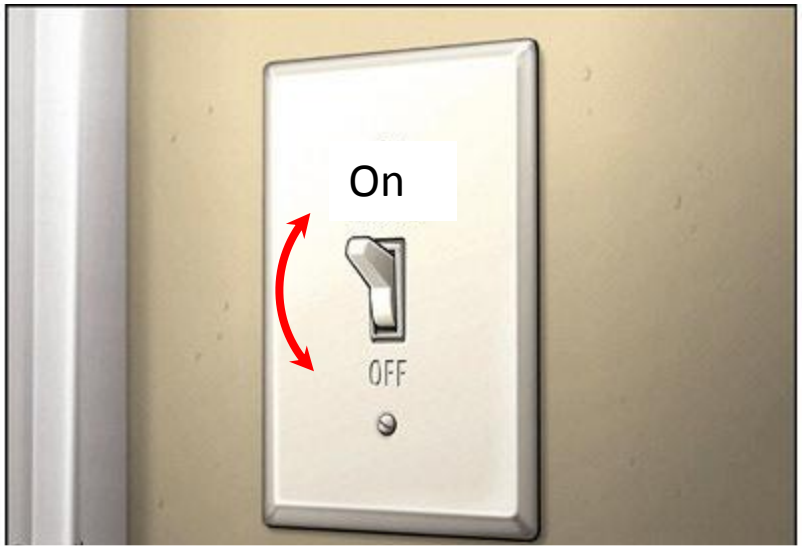
Stochastic Switching

- Stochastic Switching:

  Bistability in a stochastic framework means double peaks in the probability distribution function of concentrations. Jumping from one peak to another is possible with a finite probability.

Thermal Noise



Stochastic Gene Regulatory Network

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- Single Events: Bifurcation in Phage λ–infected E. coli. [Arkin, et al. Genetics 149 1633 (1998)]
- Multiplicative Noise Effect

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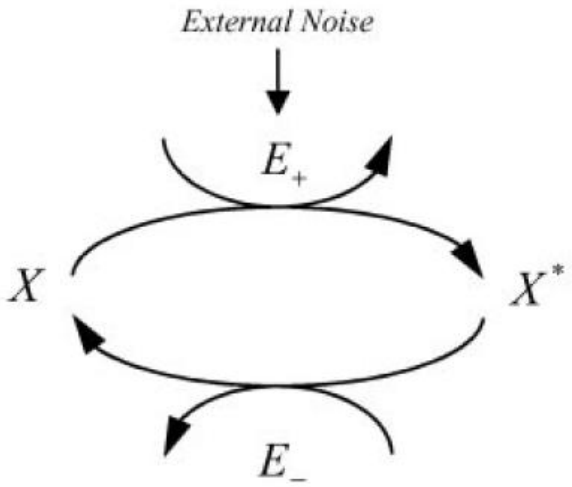
Multiplicative Noise Effect

- Multiplicative Noise: Noise strength depends on the state of the system.
- Noise-induced Bistability.
- Enzyme futile cycle reaction.

  [Samoilov, et al. PNAS 102 2310 (2005)]

  E_+ is allowed to fluctuate.

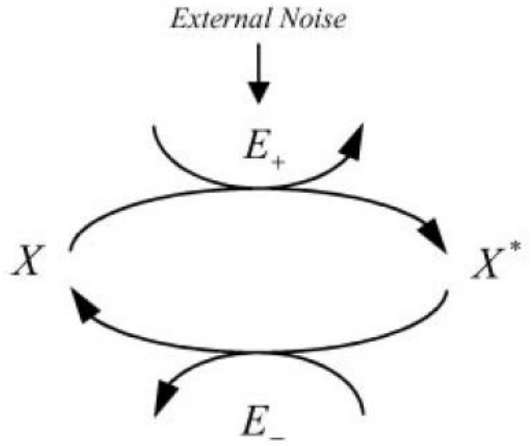


$$\nu_{X \to X^*} = \frac{E_+ X}{X + K_m},$$

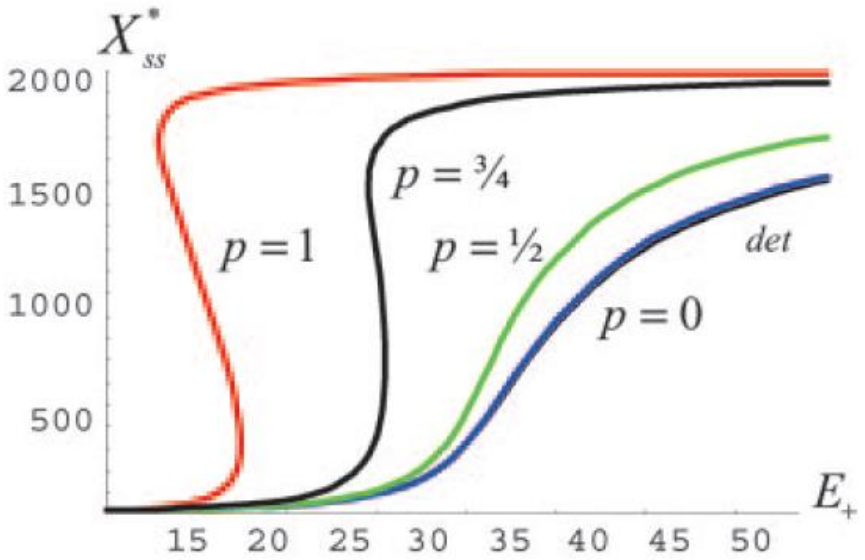
$$\nu_{X^* \to X} = \frac{E_- X^*}{X^* + K_m},$$

$$\frac{dX^*}{dt} = \nu_{X \to X^*} + \nu_{X^* \to X}.$$

Multiplicative Noise Effect



- $\mathrm{Var}[E_+] \propto \mathrm{Mean}(E_+)^{2p}$
- p=1/2 for Poisson distribution.



Multiplicative Noise Effect

- Detailed version of the enzyme futile cycle system……

p=0.96