Attenuation of Extrinsic Noise by Quorum Sensing

Yu Tanouchi[1], Dennis Tu[1], Jungsang Kim[2] and Lingchong You[1,3]

[1] Department of Biomedical Engineering,
[2] Department of Electrical and Computer Engineering,
[3] Institute for Genome Sciences and Policy,
Duke University

Introduction: cellular noise

Noise: Stochastic fluctuation of cellular molecules

Exploitation

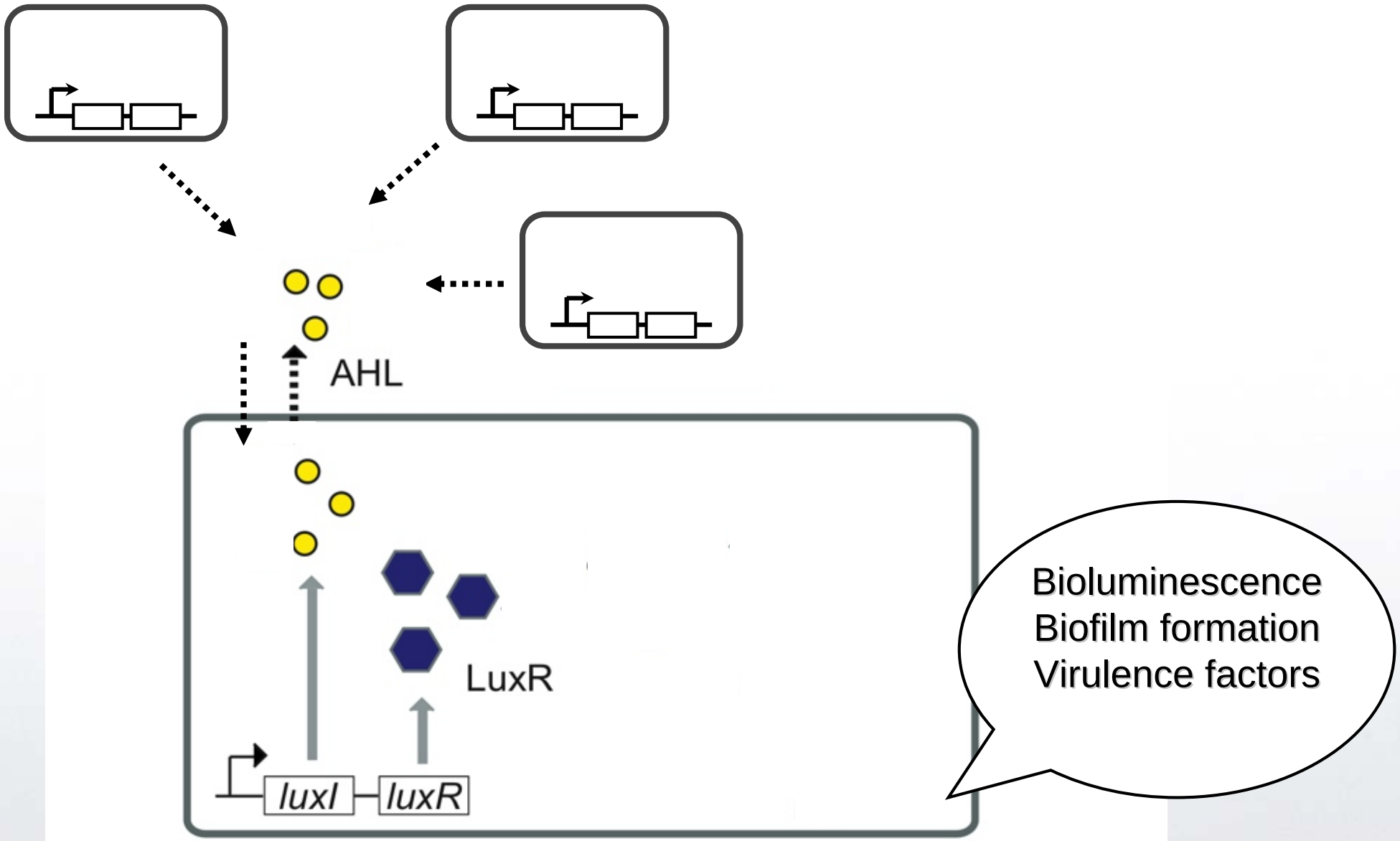
- Population heterogeneity
- Differentiation / phenotypic change
- Weak signal detection (stochastic resonance)

Attenuation

- Motifs capable of reducing noise

Intracellular level	Intercellular level
Negative feedback Ultrasensitivity Feedforwad loop	Cell-cell communication

Quorum sensing: bacterial communication



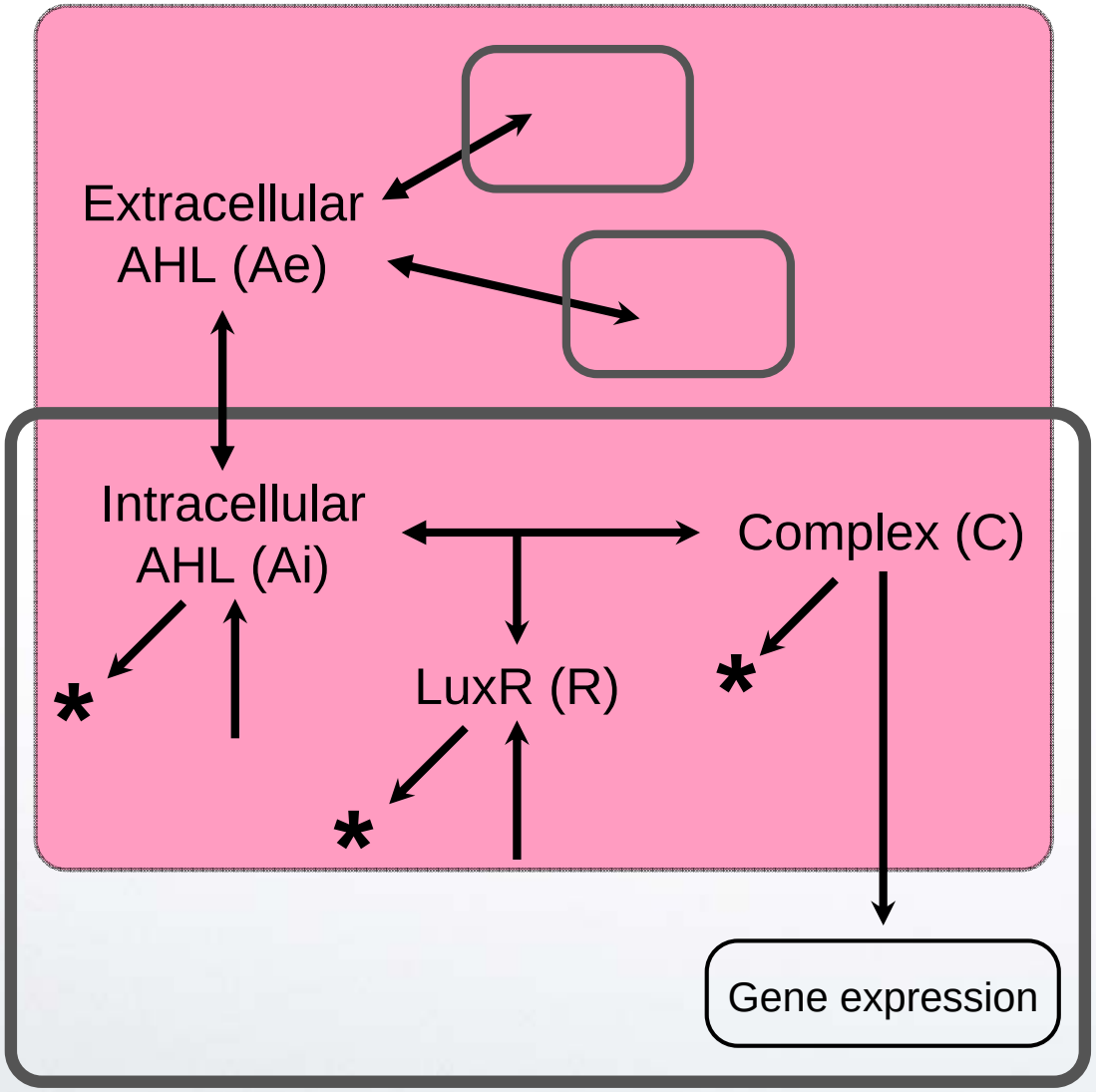
Objective

1. How does coupling between cells affect noise?

2. How does signal diffusion affect noise?
   - Signal diffusion rate across membrane corresponds to communication strength.

3. How does stability of LuxR protein affect noise?
   - LuxR-type proteins tend to be unstable when not bound to AHL
   - Is fast turnover of LuxR while waiting for AHL accumulation a waste of energy?

Model: minimal QS model



Langevin equations

$$\frac{dX_k}{dt} = f_k(\mathbf{X}(t)) + \sum_j \eta_j(\mathbf{X}(t)) + \xi$$

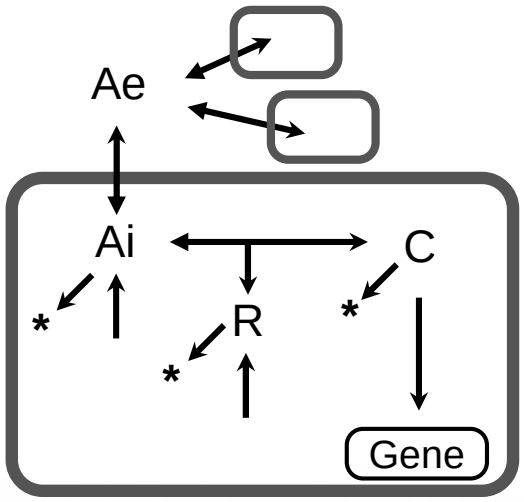
- $f_k(\mathbf{X}(t))$: Deterministic term
- $\sum_j \eta_j(\mathbf{X}(t))$: Intrinsic noise source
- ξ: Extrinsic noise source

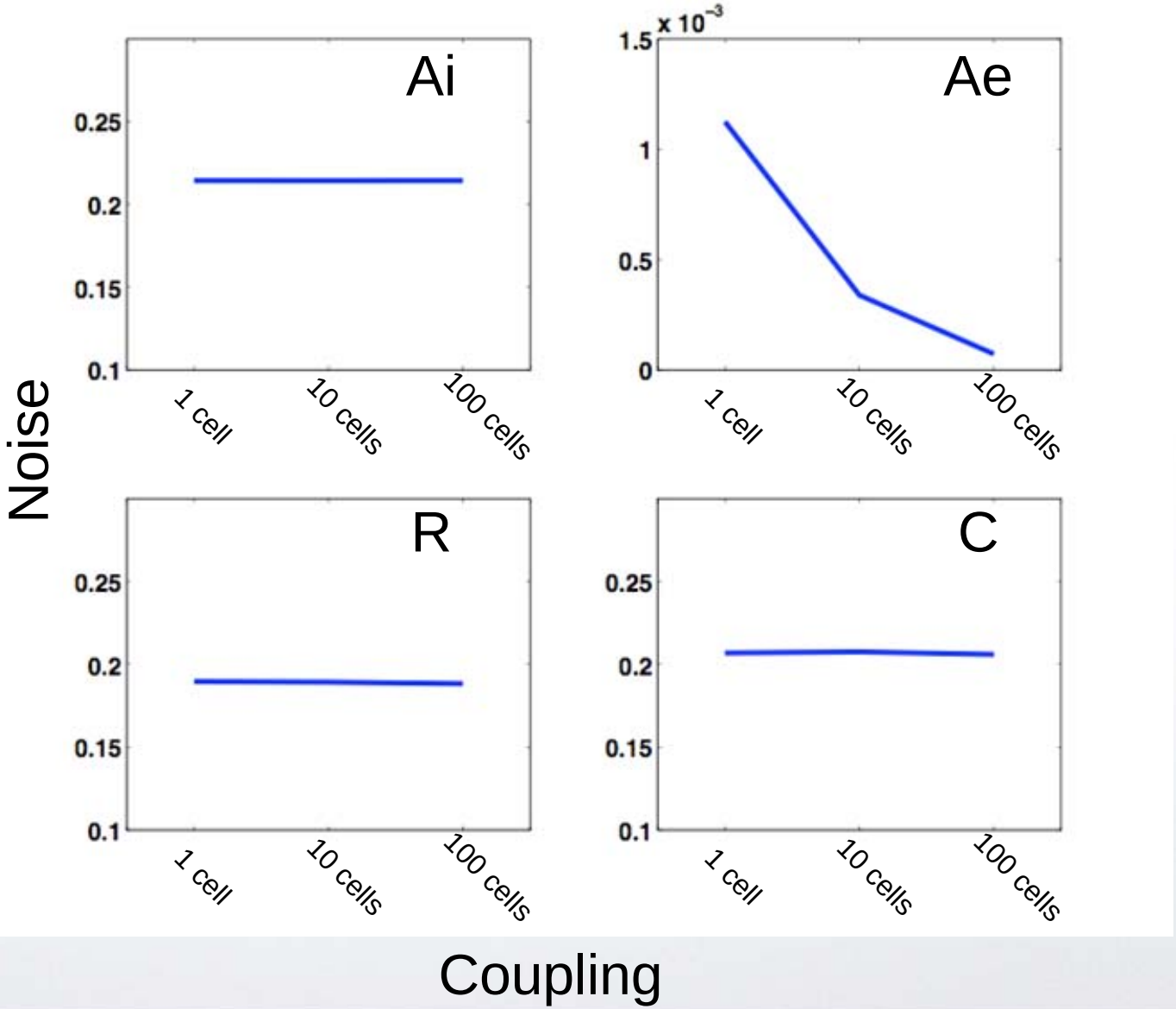
Intrinsic noise source
- -Stochastic nature of chemical reactions in the system

Extrinsic noise source
- -Fluctuations in cellular machinery outside of the system

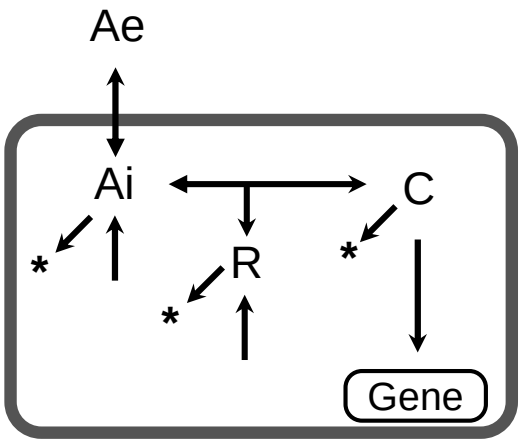
$$\text{Noise} = \frac{[\text{standard deviation}]}{[\text{mean}]}$$

Coupling has no effect on Complex





Single cell coupled with its environment



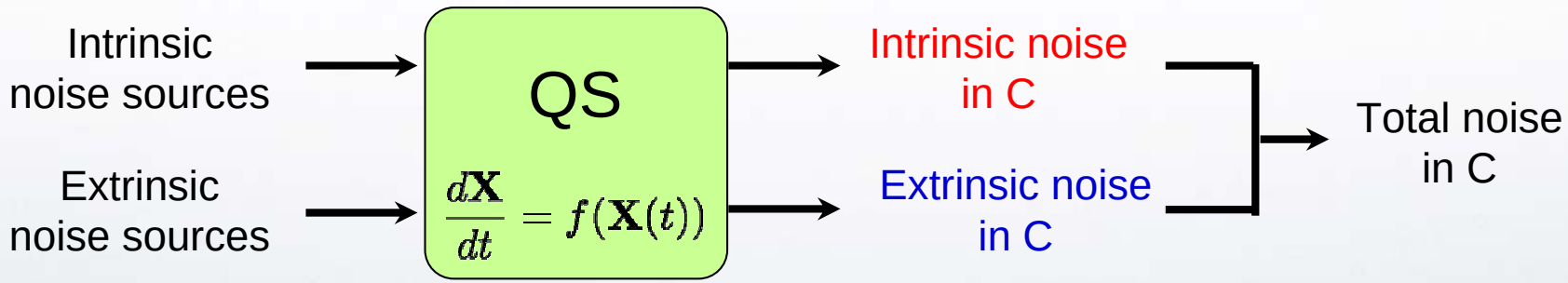
Single cell coupled with its environment

↓

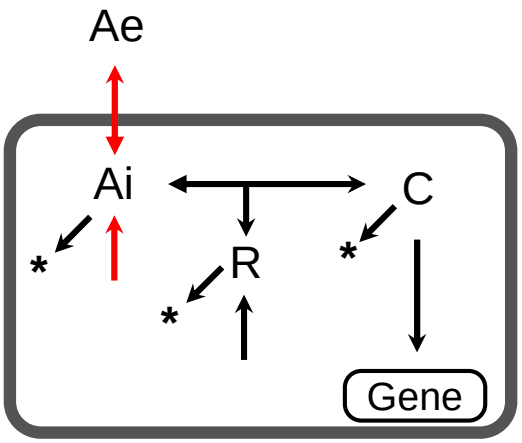
Langevin approach to solve for noise analytically

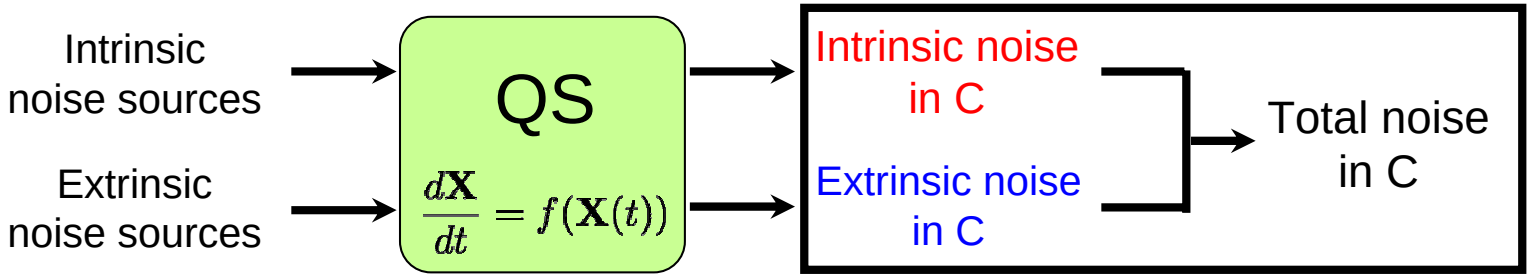
↓

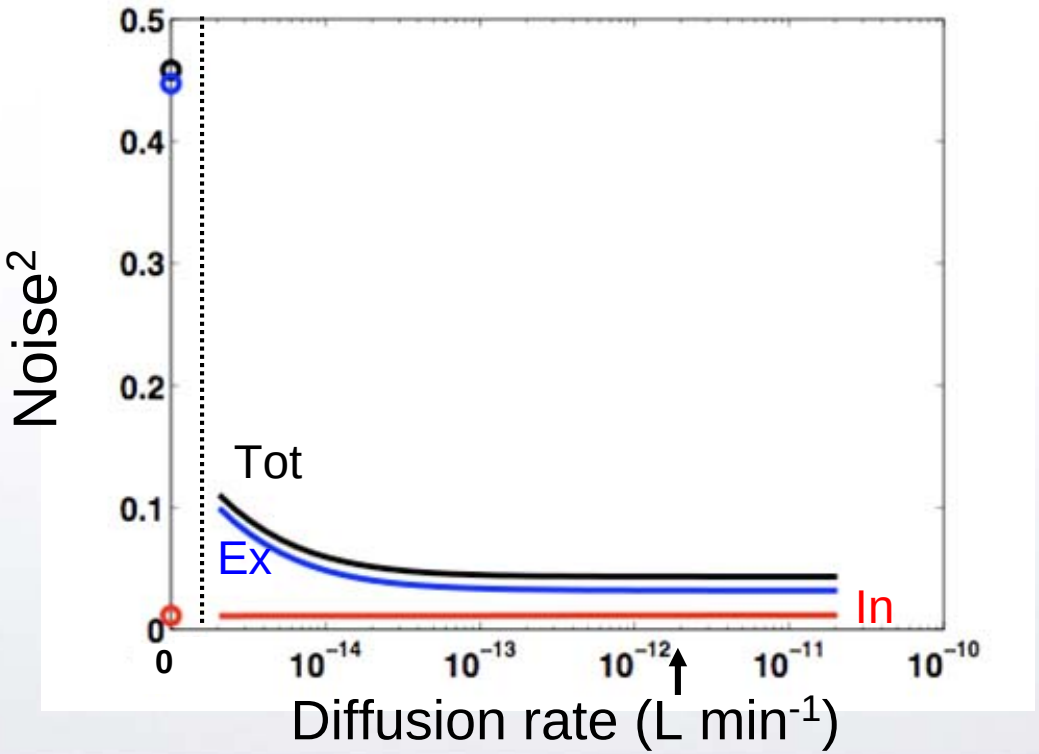
Vary signal diffusion rate / R decay rate



Fast diffusion reduces extrinsic noise



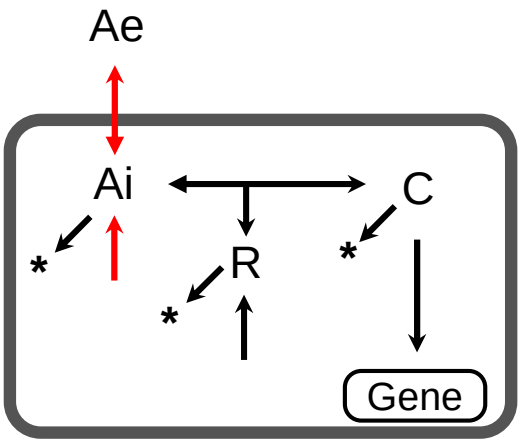


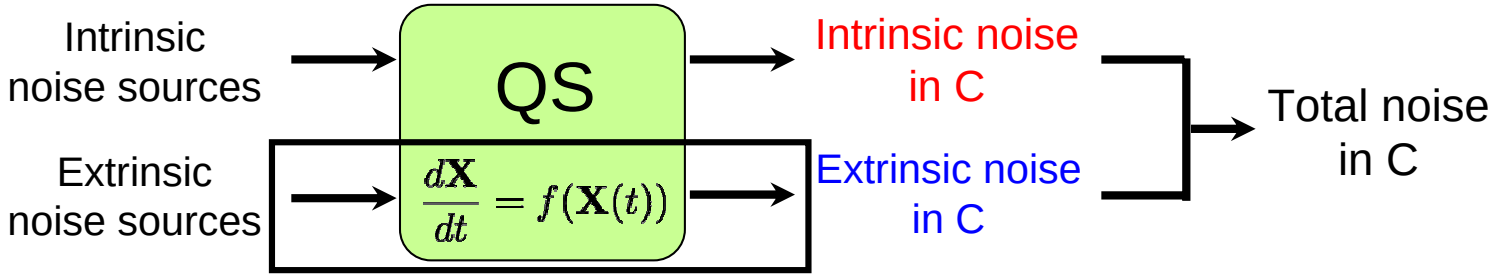


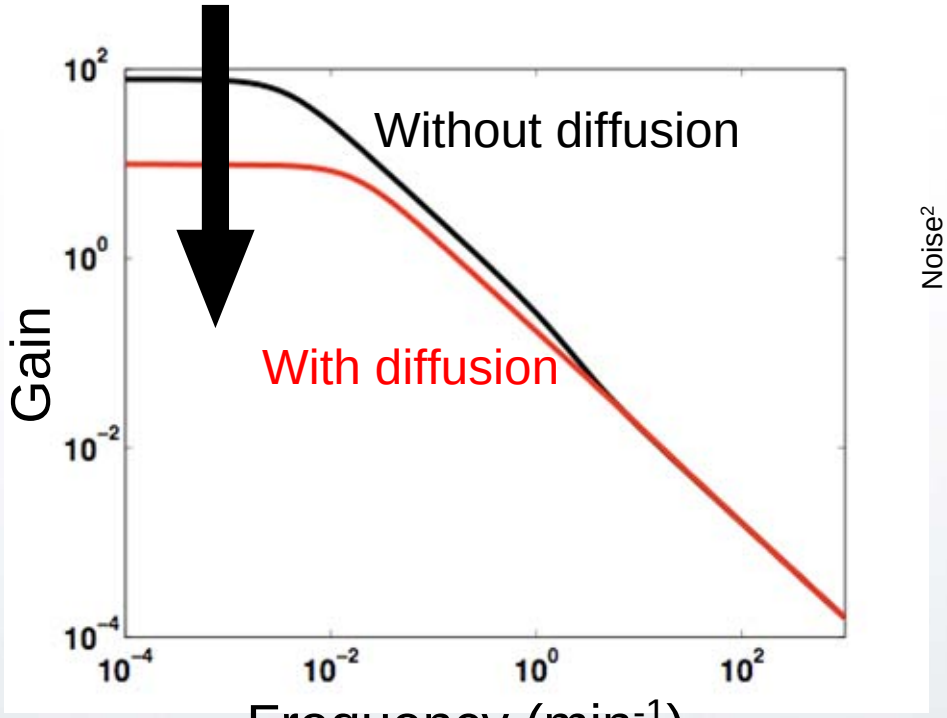
↑ : Base value

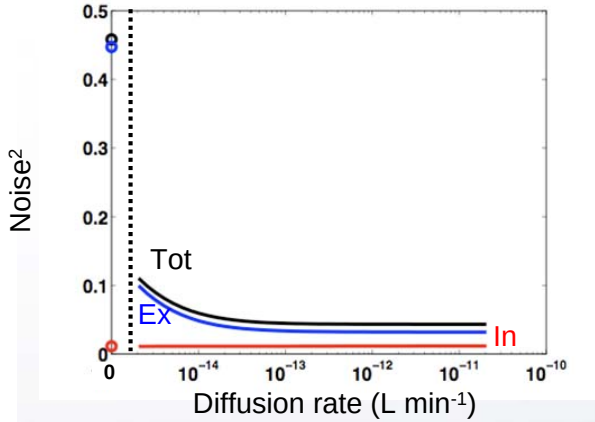
How does this extrinsic noise attenuation happen?

Extrinsic noise is attenuated in low frequency



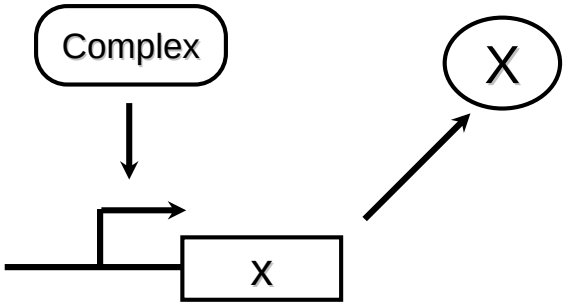






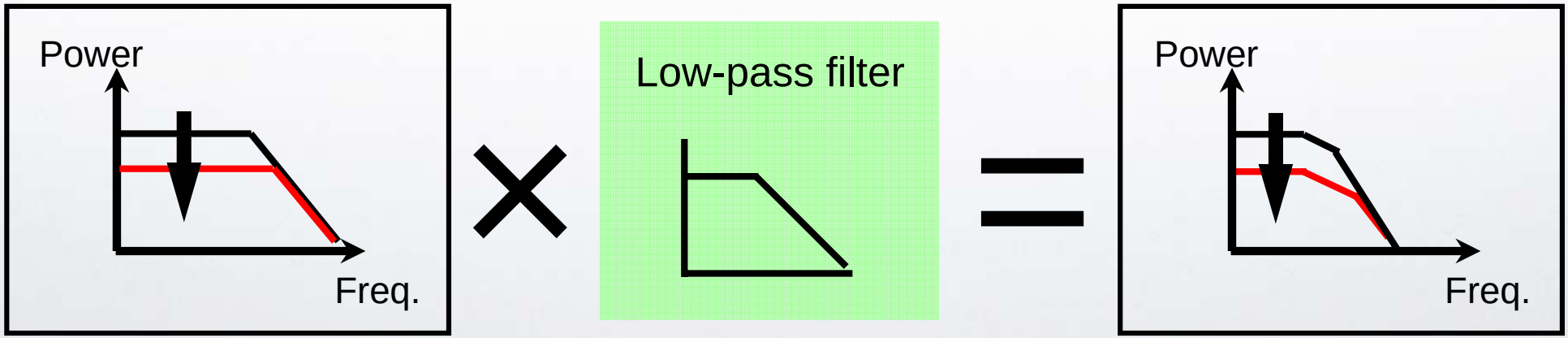
The same is true for fast R decay

Attenuation of low-frequency range is transmitted to downstream gene expression

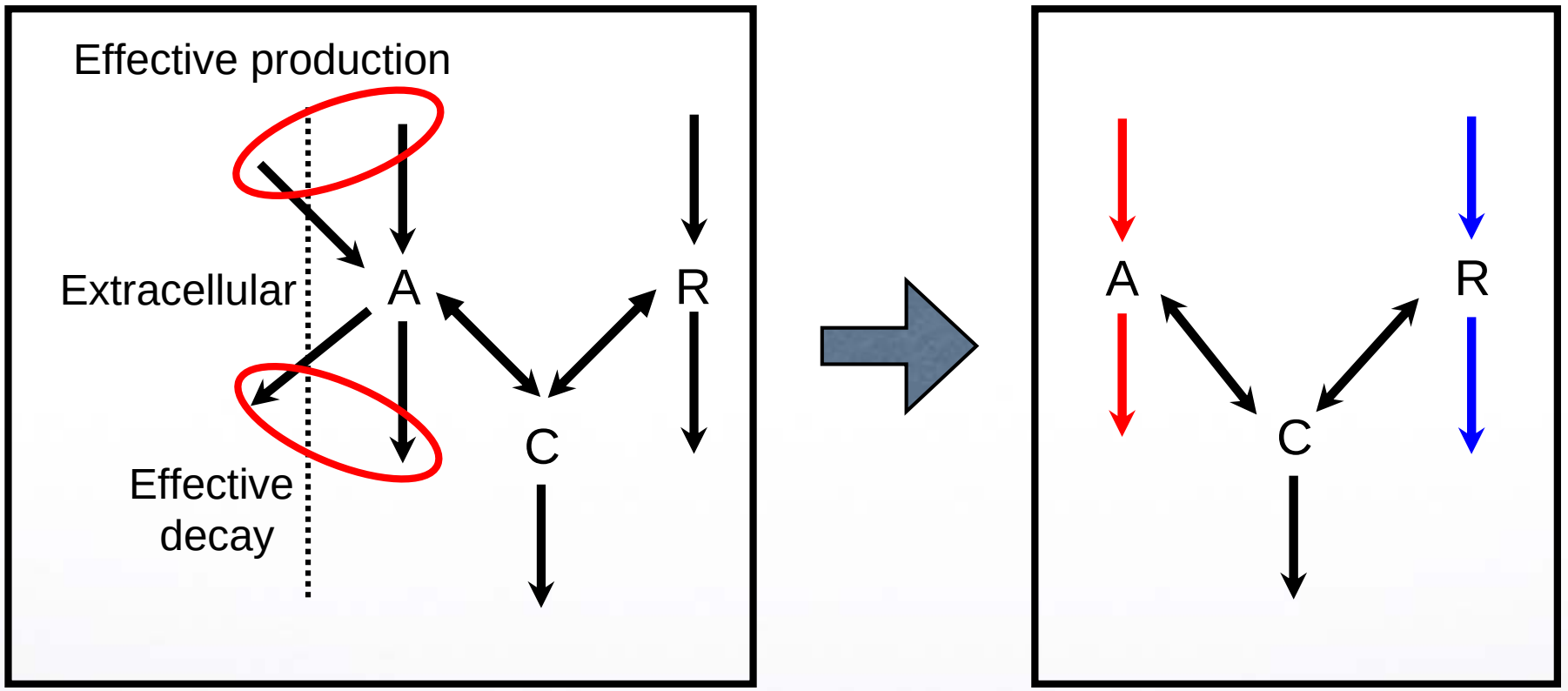


Gene expression machinery works as a low pass filter

Noise in Complex → Gene Expression → Noise in X from noise in Complex



Quorum sensing: special case of more generic motif



- Fast turnover of A and R leads to extrinsic-noise attenuation
- Diffusion is one specific mechanism to achieve fast turnover of A

Summary

- Fast diffusion and R decay attenuate extrinsic noise.
- Noise attenuation is achieved by reducing low-frequency components which can be effectively transmitted to downstream gene expression.
- Quorum sensing is one implementation of the heterodimerization motif.

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