

All chemical reactions are affected by thermal fluctuations and so are stochastic

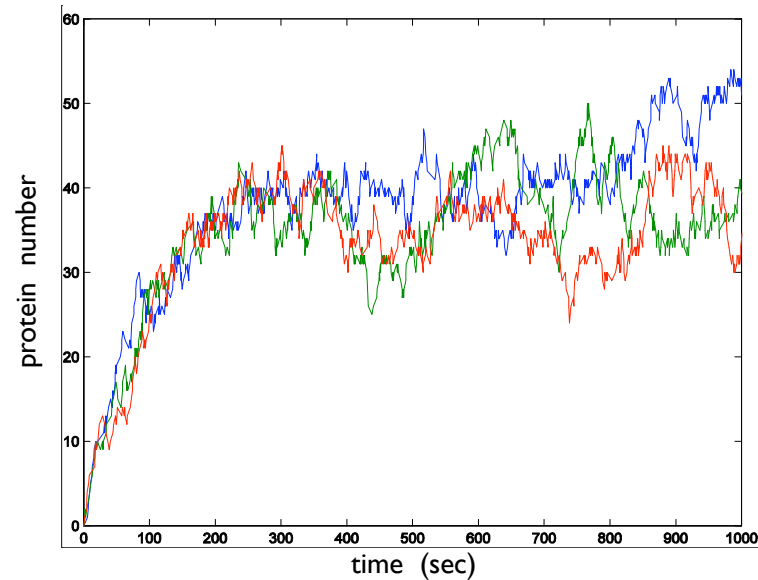


1. Reactants diffuse to find each other in solution
2. They must overcome the energy barrier of the reaction

Both events are randomly affected by thermal fluctuations – collisions with other molecules.

If the numbers of molecules are sufficiently large, then the mean number of molecules or, more correctly, the mode approximately obeys the appropriate rate equations.

How should we quantify stochasticity?

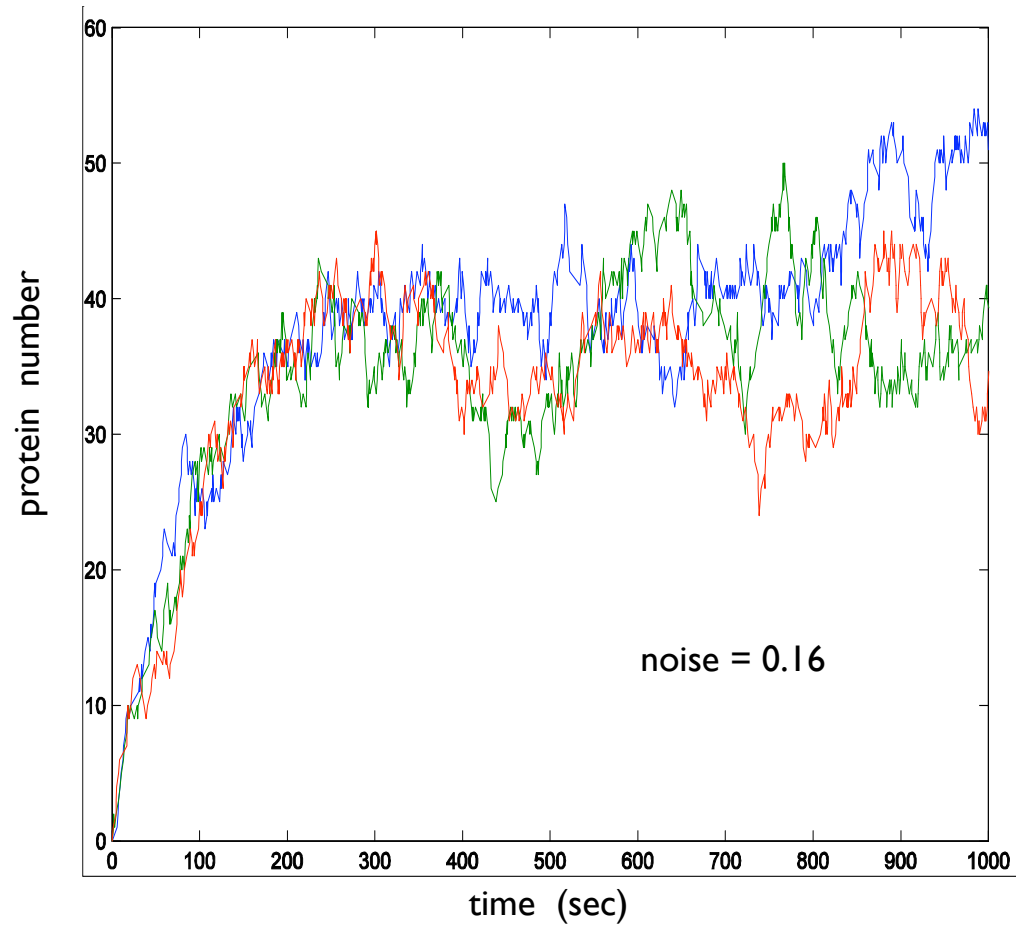


Noise is often defined as the coefficient of variation – the typical size of a fluctuation relative to the mean:

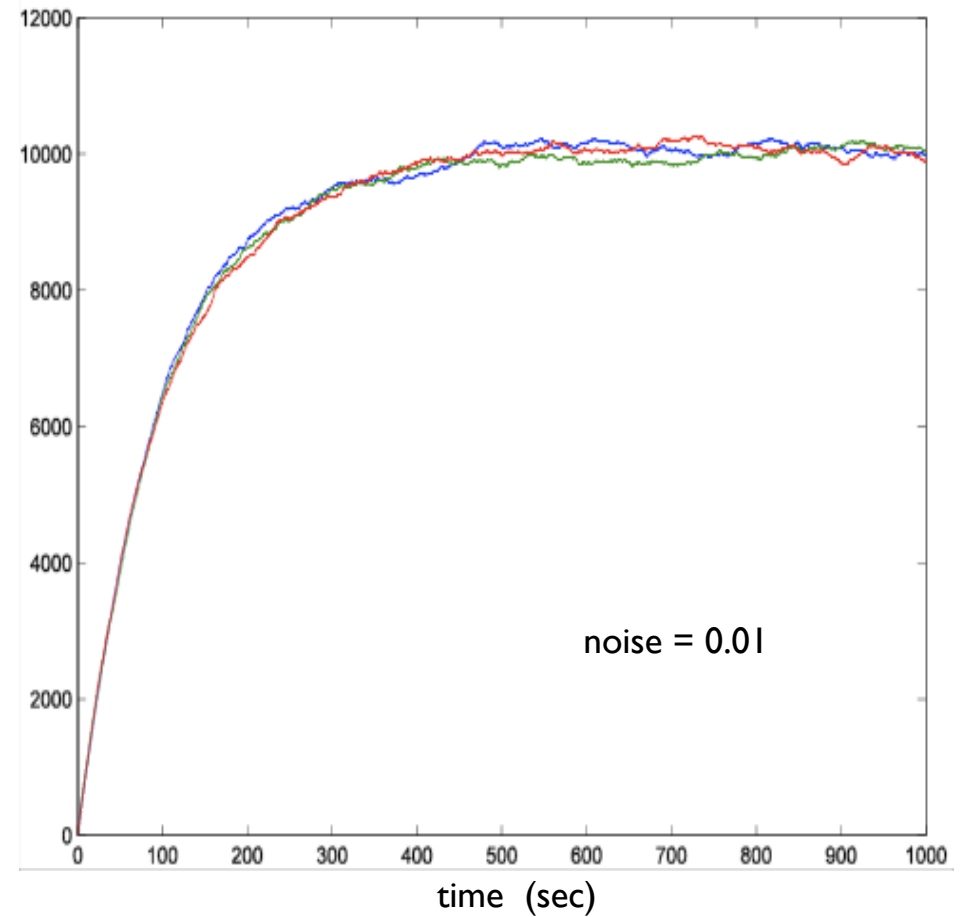
$$\text{noise} = \frac{\text{standard deviation}}{\text{mean}}$$

Stochasticity is more substantial at low numbers. Why?

mean 40



mean 10,000

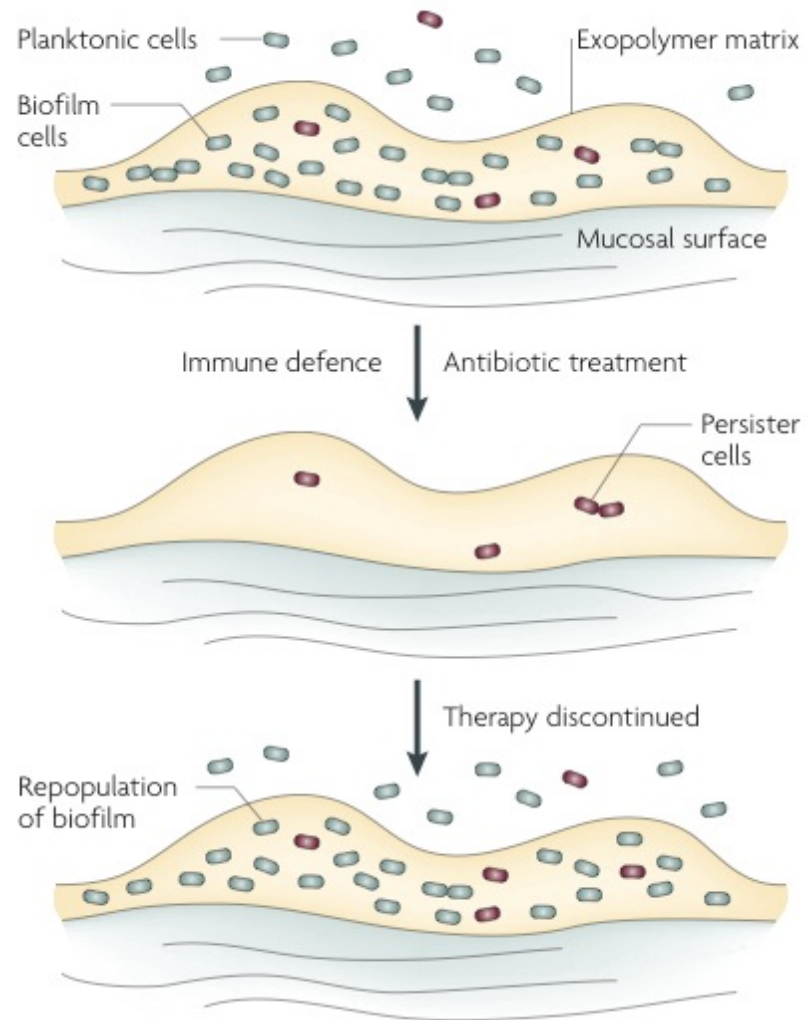


Why is stochasticity only substantial when typical numbers of molecules are low?

As a reaction changes the number of molecules by one or two, it is only when numbers are small that stochasticity – the random timing of individual reactions – matters.

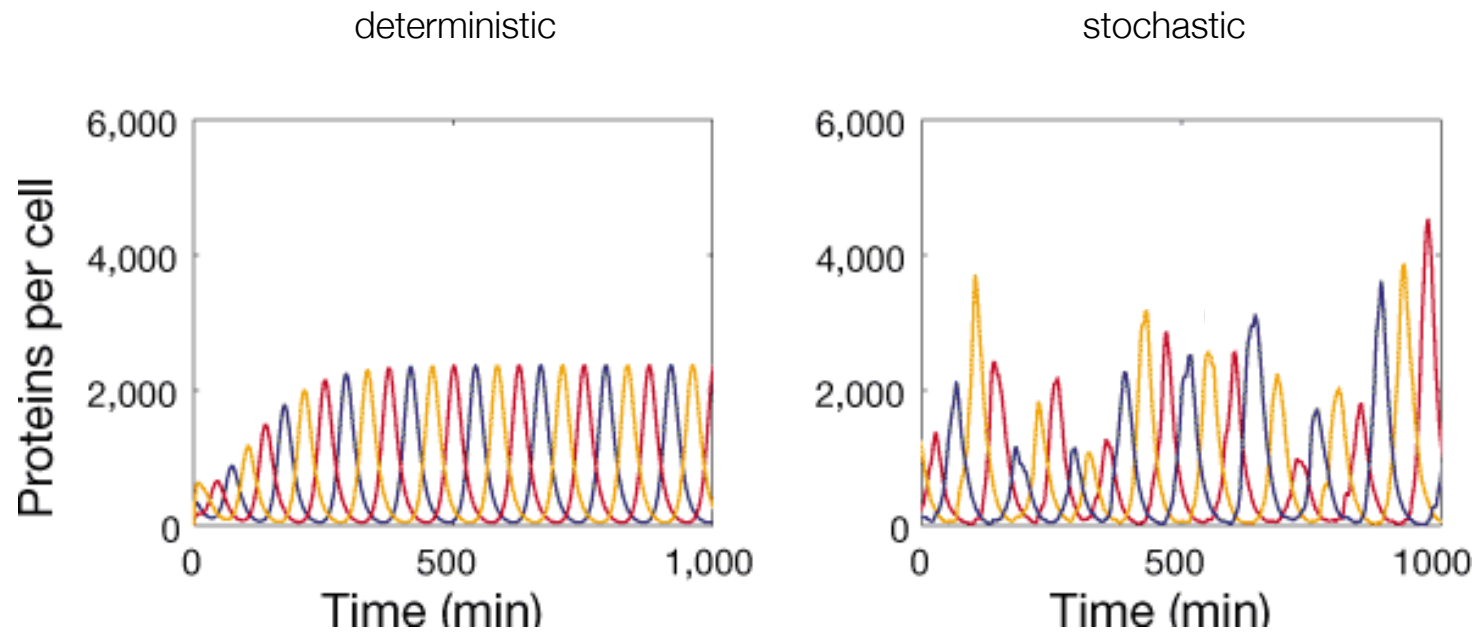
Stochasticity can be exploited: persister cells enable a population to be both invasive and tolerant to drugs

probability of
being a
persister is less
than 10^{-5}
for *E coli*



Stochasticity affects the reliability of biochemical networks by affecting timing and is therefore regulated away

e.g. biological rhythms

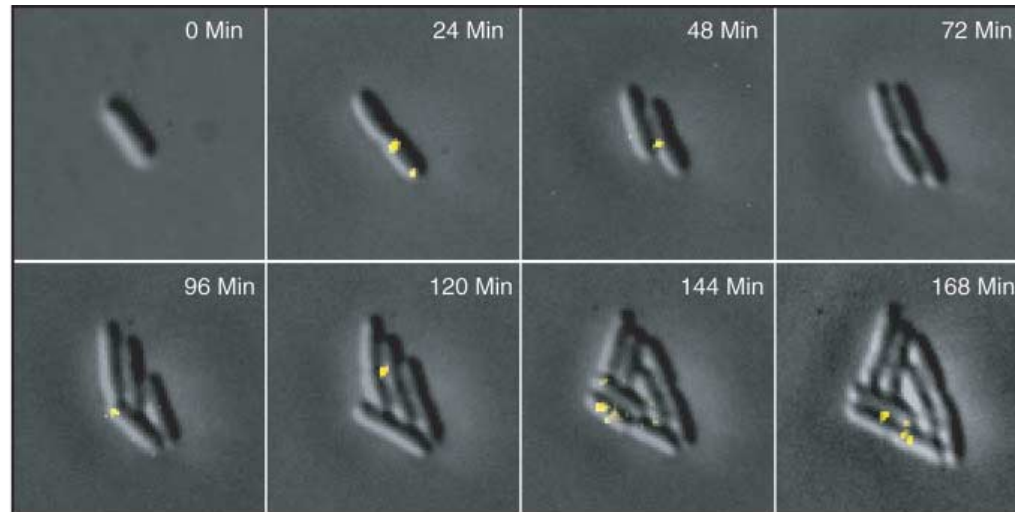


Stochasticity is generated during gene expression: translation can occur in bursts

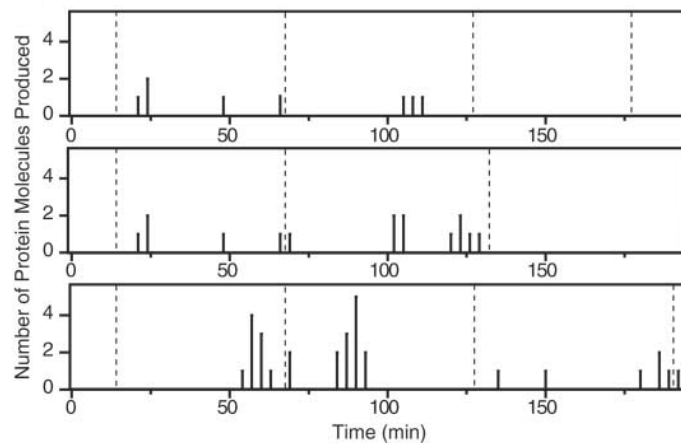
Probing Gene Expression in Live Cells, One Protein Molecule at a Time

Ji Yu,^{1*} Jie Xiao,^{1*} Xiaojia Ren,¹ Kaiqin Lao,² X. Sunney Xie^{1†}

Following expression of a fluorescent membrane protein in bacteria over time.



Occasionally, one mRNA is transcribed.



Bursts of translated protein.



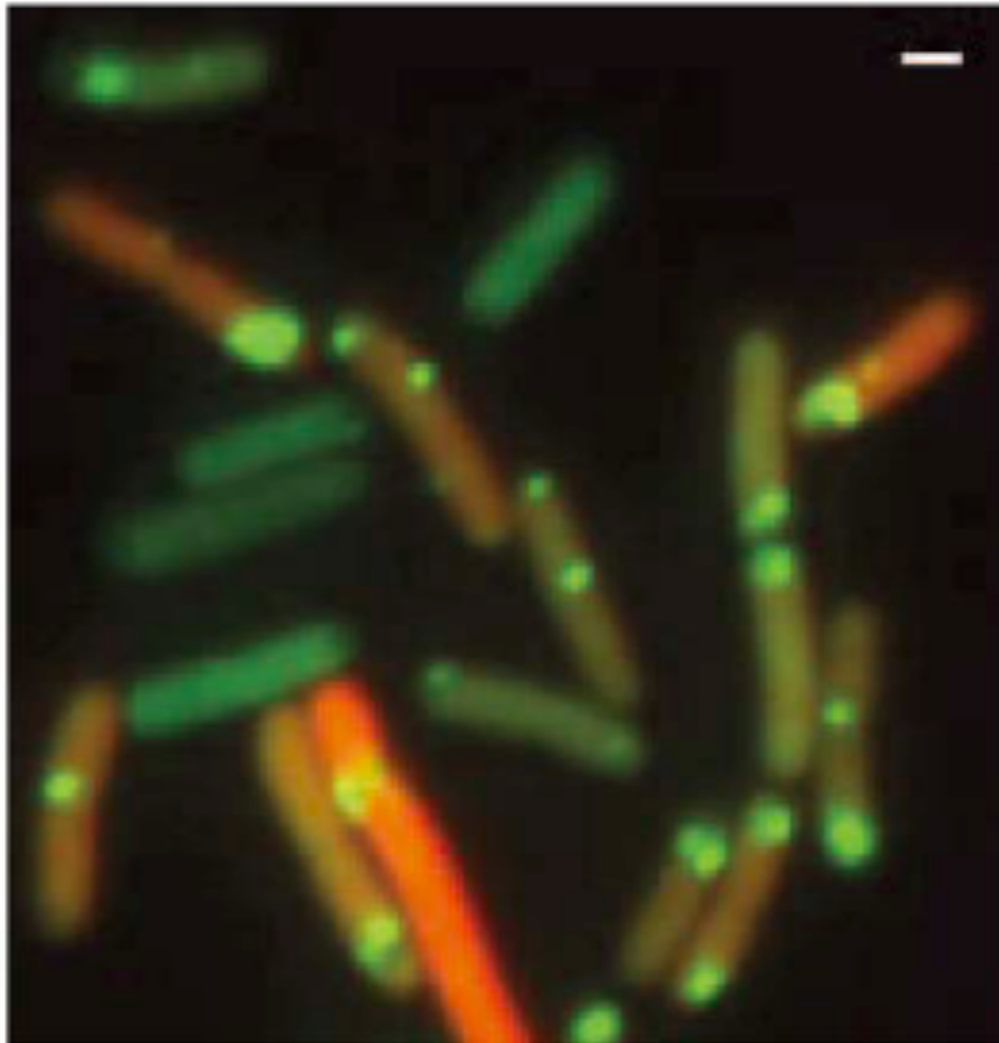
Yu *et al.*, Science (2006)

Transcription can also occur in bursts

Real-Time Kinetics of Gene Activity in Individual Bacteria

Ido Golding,^{1,*} Johan Paulsson,^{2,3} Scott M. Zawilski,¹ and Edward C. Cox^{1,*}

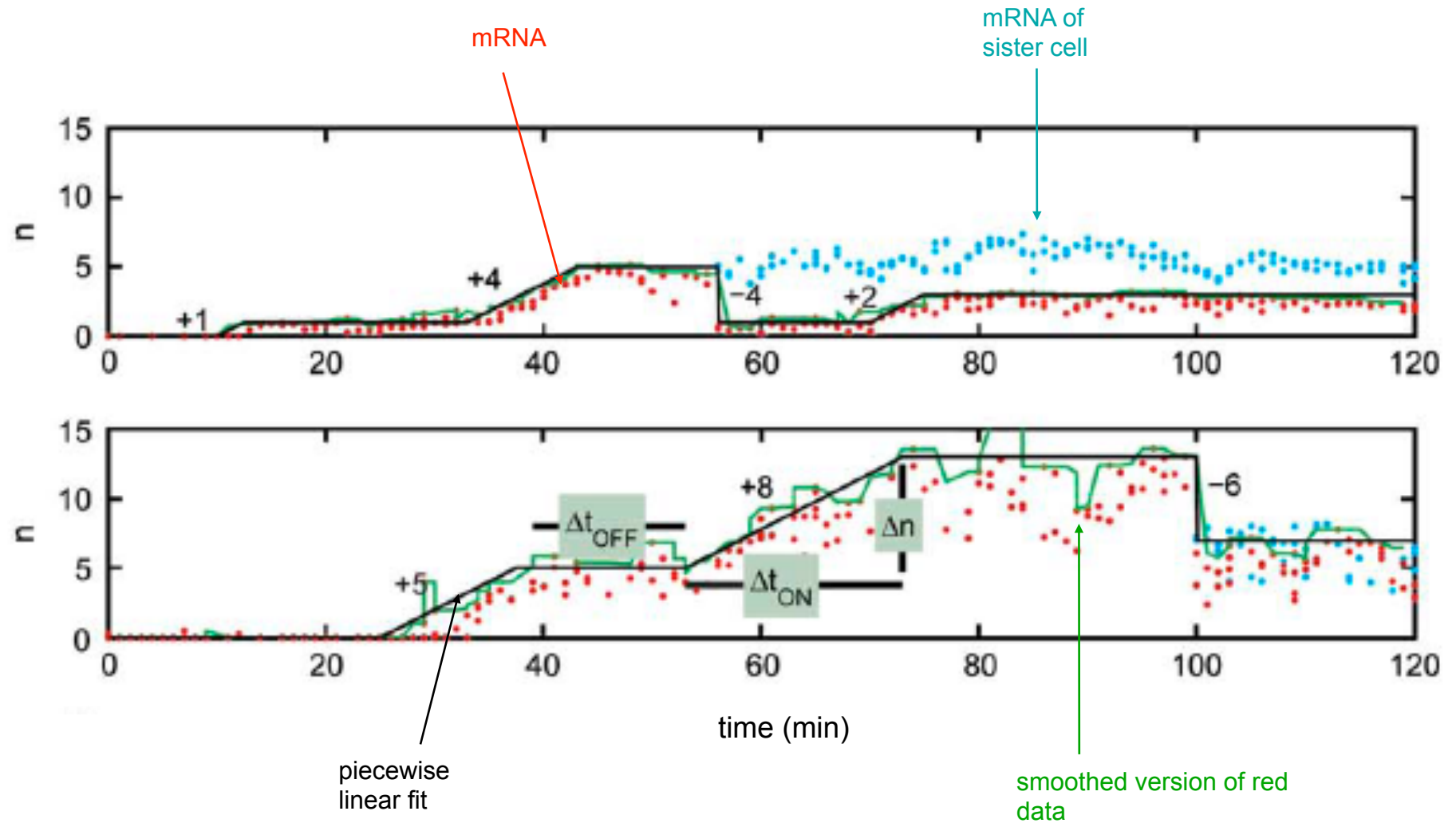
Cell 123, 1025–1036, December 16, 2005



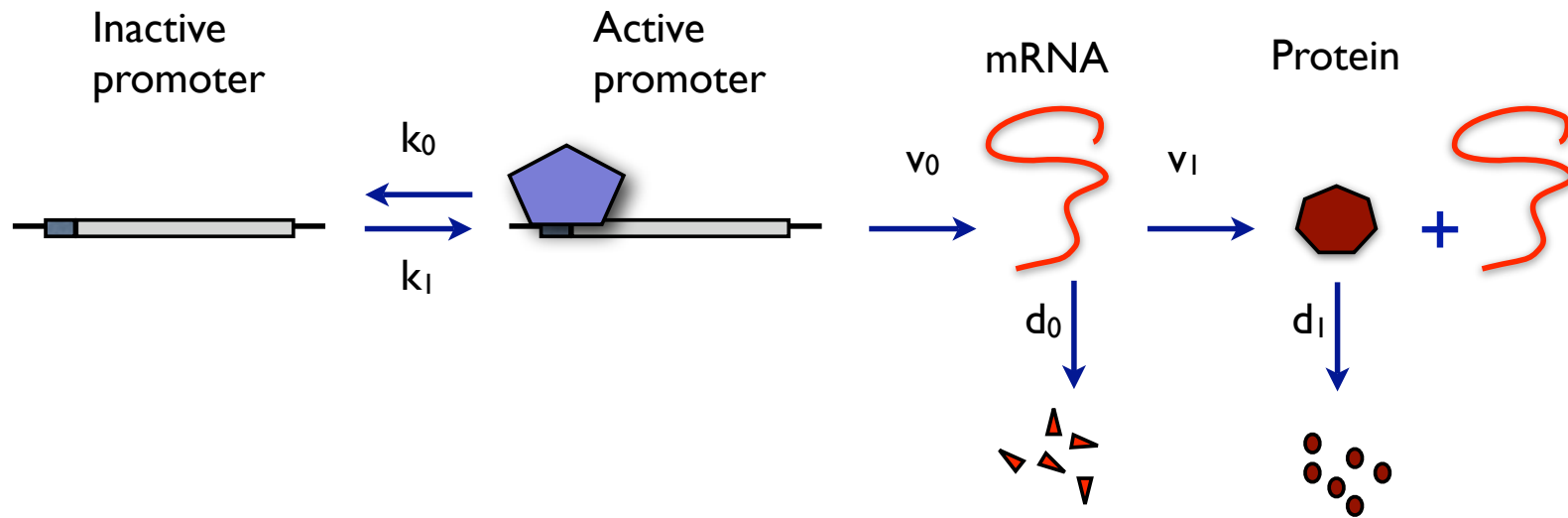
Red: protein
Green spots: mRNA

scale bar: 1 μm

Time course of mRNA numbers: mRNA is produced in bursts



The most common model of gene expression has both bursts in transcription and translation

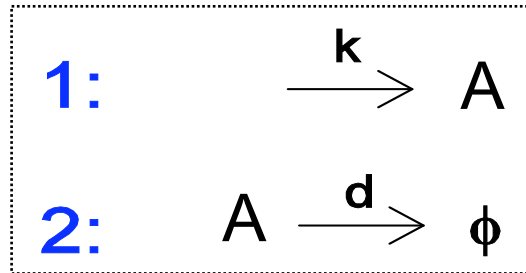


To perform stochastic simulations, we typically use the Gillespie, or stochastic simulation, algorithm

Step 1: choose which reaction will occur

Step 2: choose when that reaction will occur

Example: an elementary model of gene expression



probability of a reaction in time δt

$$a_1 \delta t = k \delta t$$

propensity of reaction 1

$$a_2 \delta t = dA \delta t$$

propensity of reaction 2

probability of no reaction

$$P_0(t + \delta t) = P_0(t) \left[1 - (a_1 + a_2) \delta t \right] \quad \text{hence} \quad P_0 \sim e^{-(a_1 + a_2)t}$$

probability of a reaction i at time $t + \delta t$

$$P_i(t) \delta t = P_0(t) a_i \delta t$$