Stochastic Modelling in Systems Biology

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MRes Systems & Synthetic Biology

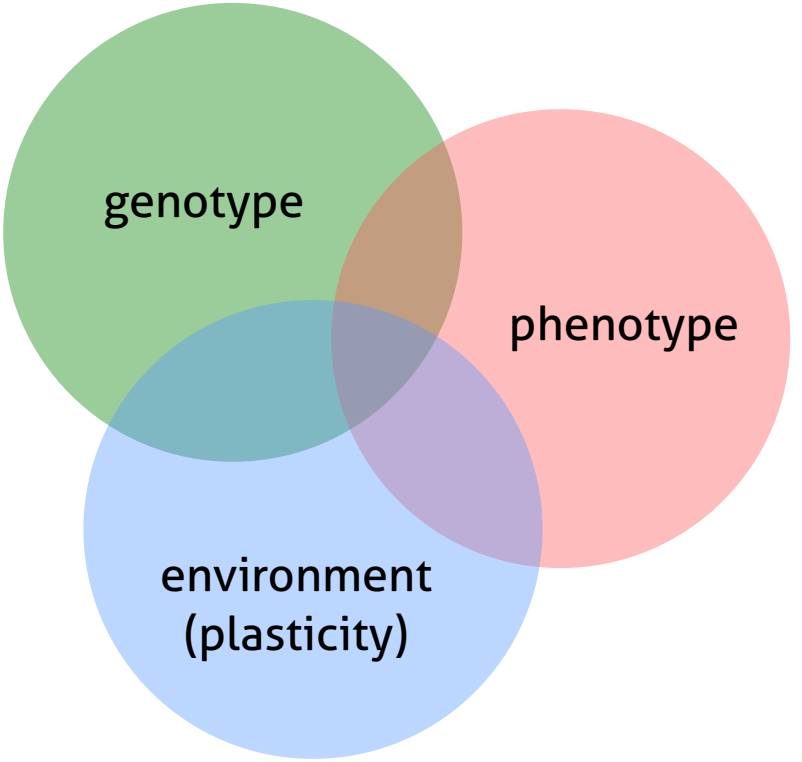
Stochastic Modelling in Systems Biology

I) Stochasticity in biosystems

II) Stochastic Simulation Algorithm

III) Chemical Master Equation

Biological variability



complexity of biological variation

Biological variability

Fingerprints of identical twins
are readily distinguished on close examination.

Biological variability

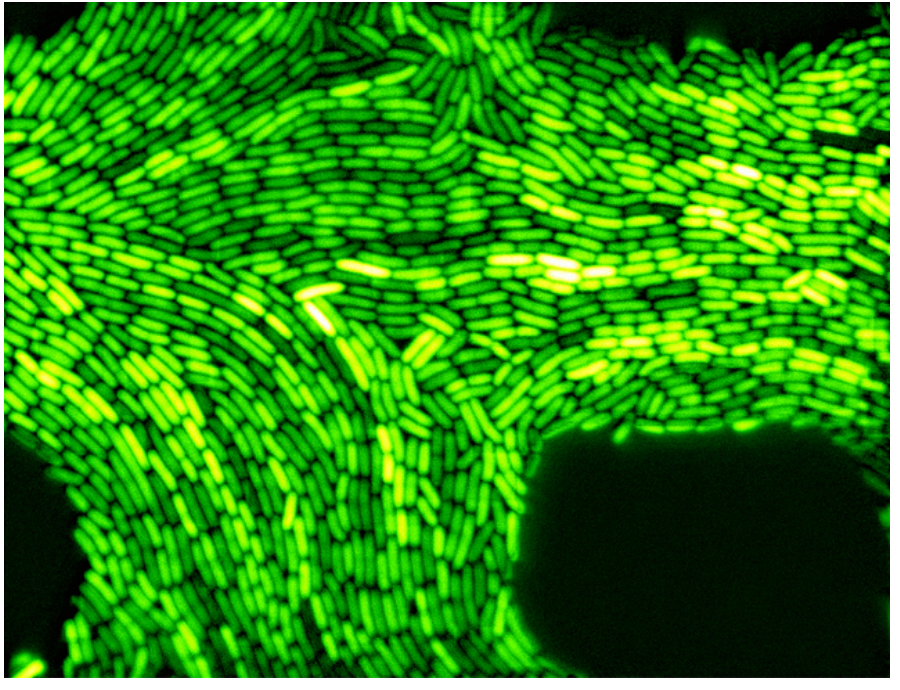
Cc, the first cloned cat (left) and Rainbow, Cc's genetic mother (right), display different coat patterns and personalities.

Biological variability

Genetically identical organisms can have different appeareances.

What is the orgin of these phenotypic differences?

We often use simple model organisms to understand these questions



Microscopy image of *Escherichia coli* population

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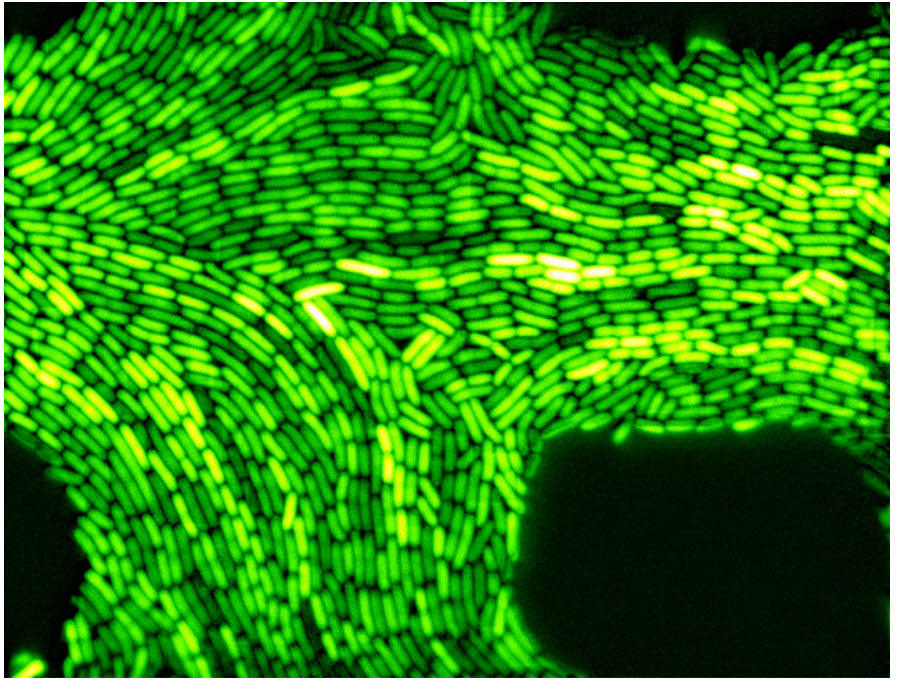


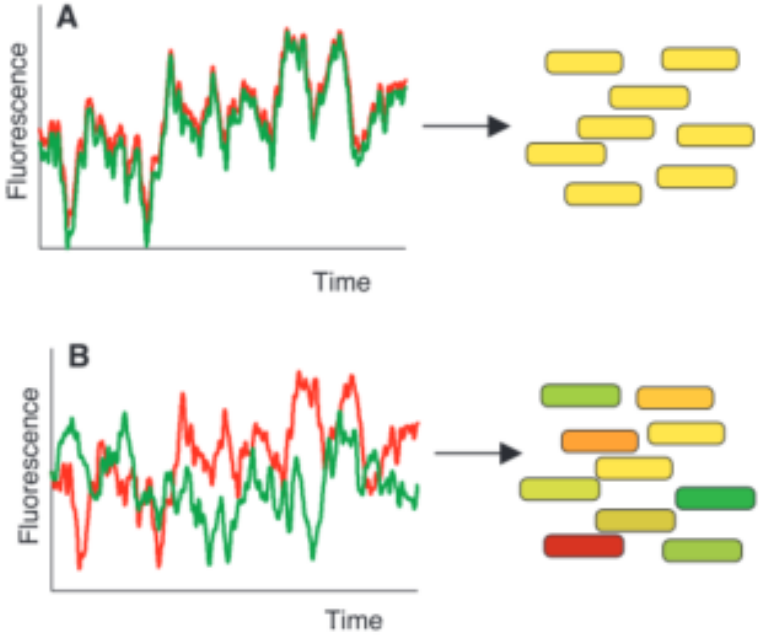
Microscopy image of *Escherichia coli* population

Genetically identical bacteria produce varying amounts of green fluorescent protein.

Technical term is **noise** (defined later), which is caused by gene expression.

How to prove it?

Two-reporter system:
identical gene copies on different positions of the chromosome



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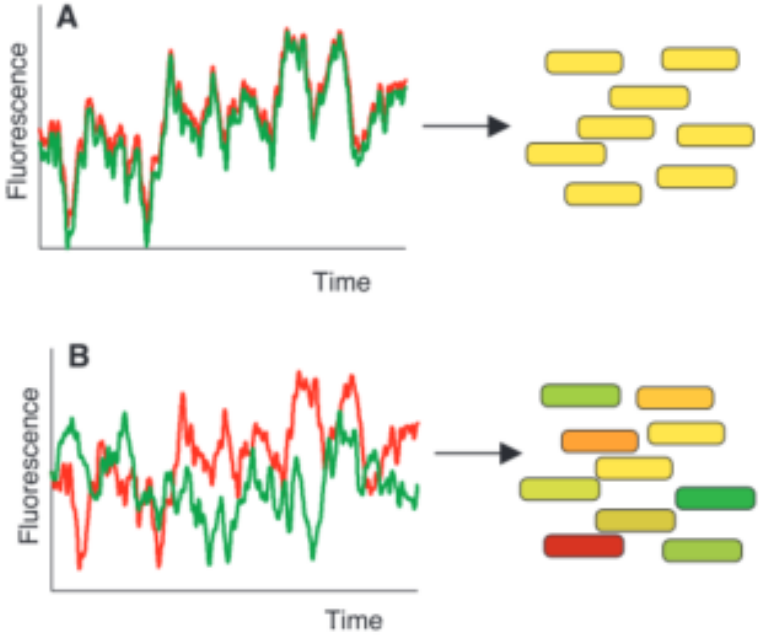
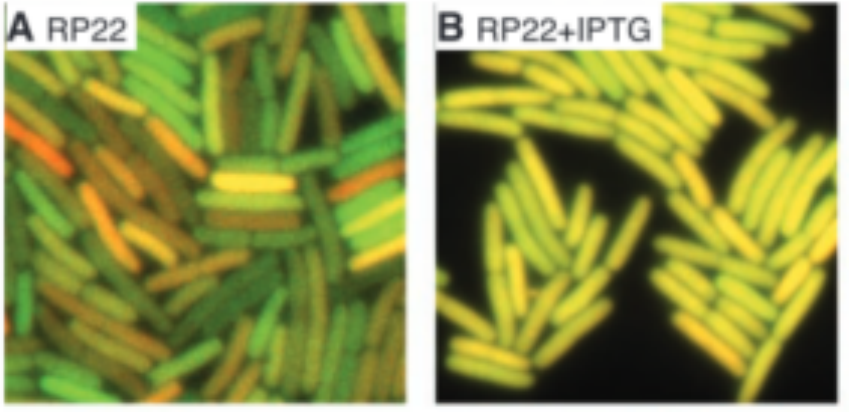
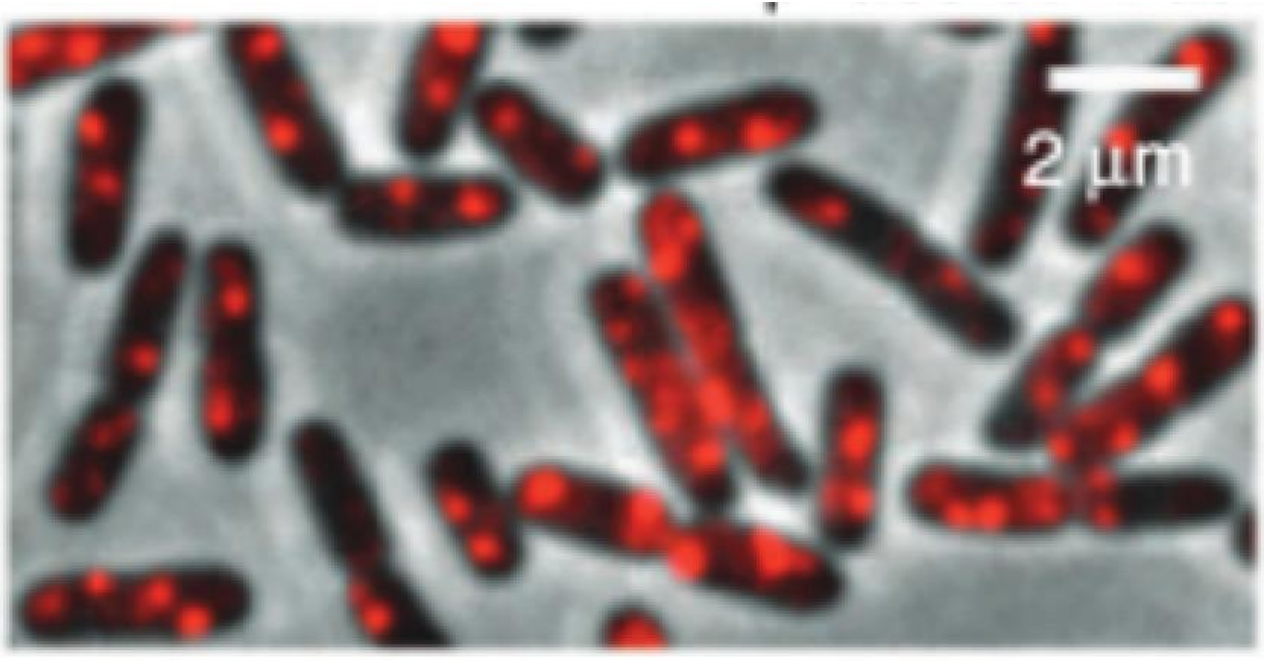




Elowitz, M.B., Levine, A.J., Siggia, E.D. and Swain, P.S., 2002. Science, 297, 1183-1186.

Experimental mRNA quantification

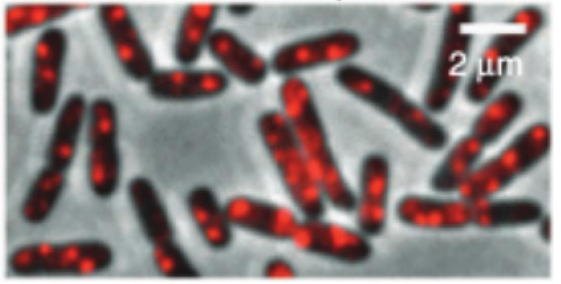


Single molecule FISH makes individual mRNA molecules visible.

So et al. (2011) Nat Genet 43, 554–560

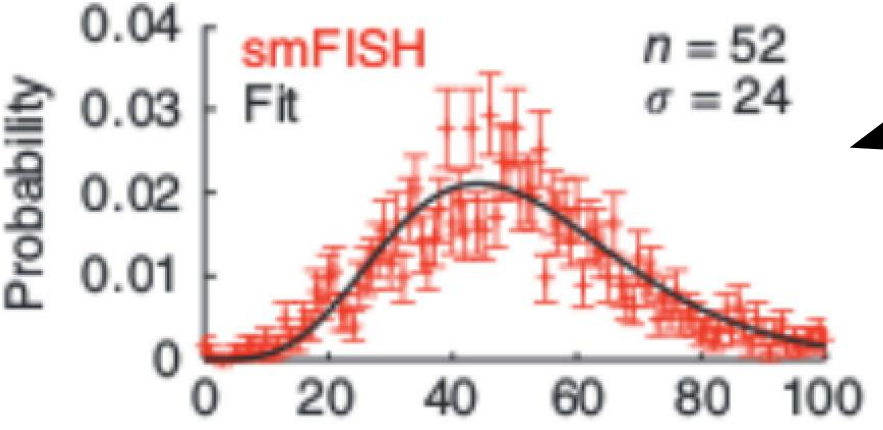
Counting molecules: one by one, cell by cell

Single molecule FISH detects single mRNA molecules in cells



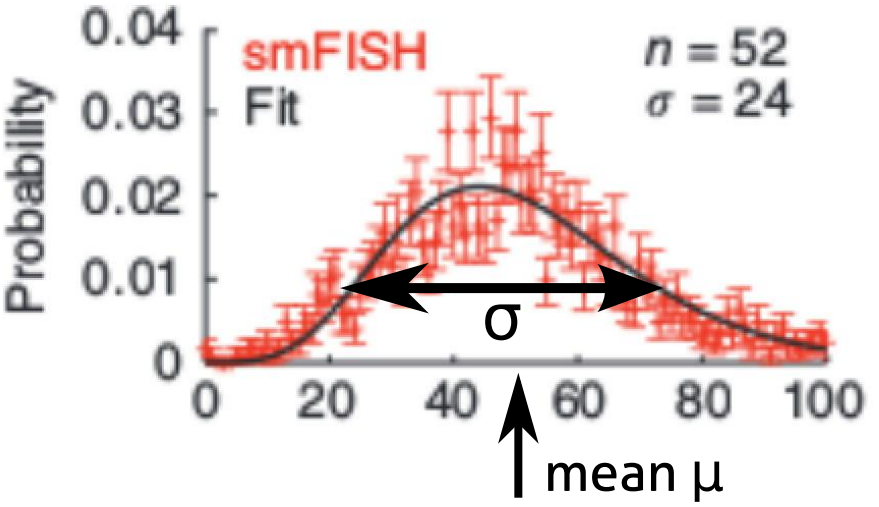
Count number of spots in the cell

Probability of having n molecules =
no. of cells with n molecules/total no. of cells



most cells have between 40-50 mRNA molecules
but a lot of cells have much more or less

Quantitative biologists use summary statistics

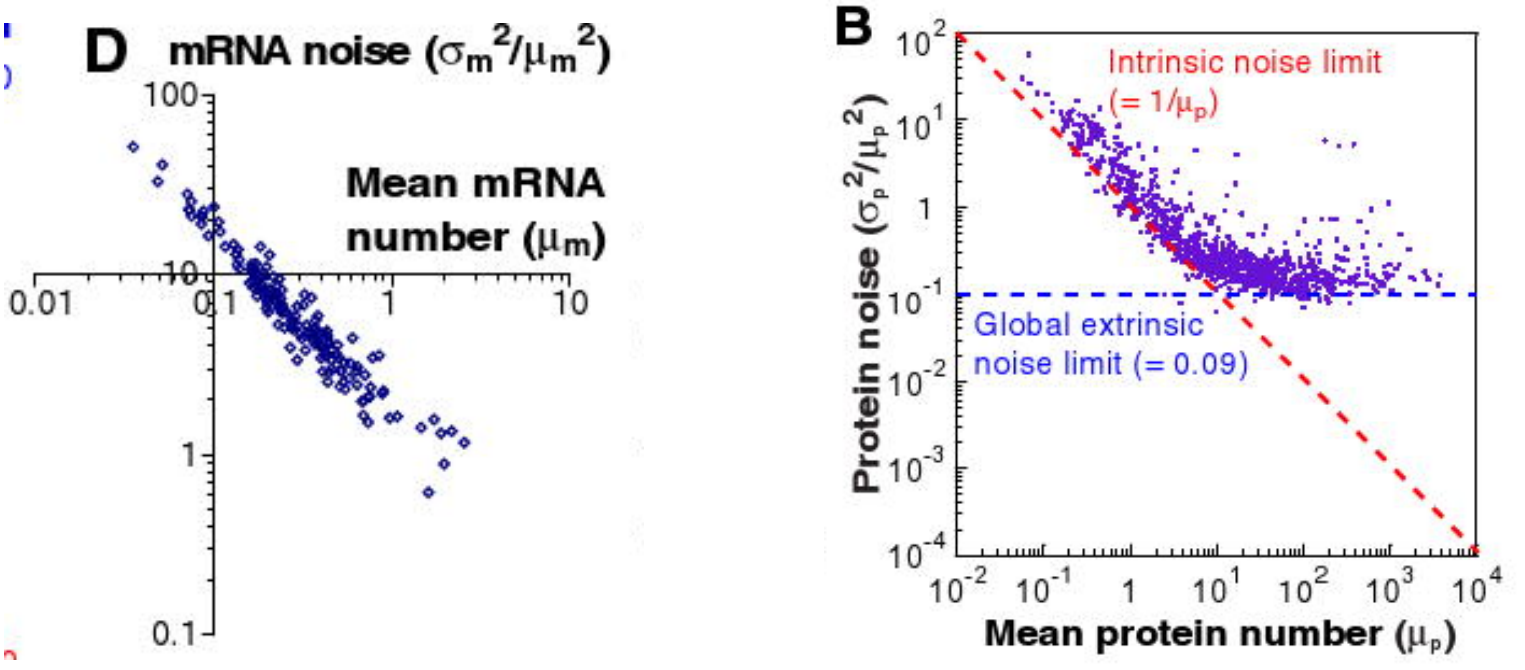


mean molecule number $\mu=52$

standard deviation $\sigma=24$ → coefficient of variation measures the **size of the noise** or relative spread of the distribution $\sigma/\mu \approx 1/2$

molecule numbers vary about 50% from their mean values

Genome-wide studies of molecular noise



Noise decreases with molecule abundance.

Many genes are expressed in few mRNAs or protein molecules and thus plays important role in many cellular processes..