Intrinsic variability in exponentially growing systems

June 9, 2022

The simple birth (Yule) process

We consider a pure birth Markov process with $B_n = \mu n$.

The master equation for this process has a solution $P_{ij}(t)$ (prob. that a system initialized in state i is in state j at time t):

$$P_{ij}(t) = \frac{\mu(i+j-1)!}{(i-1)!(j-1)!} e^{-it\mu}(1-e^{-\mu t})^{j-1}, \quad \text{if } j > i$$

and

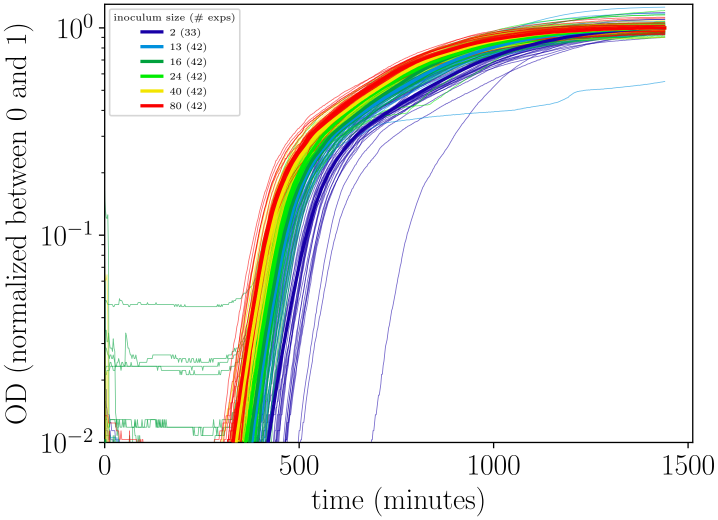
$$P_{jj}(t) = \mu j \, e^{\mu j t}.$$

The first-passage time distribution $\tau_{ij}(t)$ of times at which a system initialized in state i first reaches state j is related to $P_{ij}(t)$ according to the renewal equation:

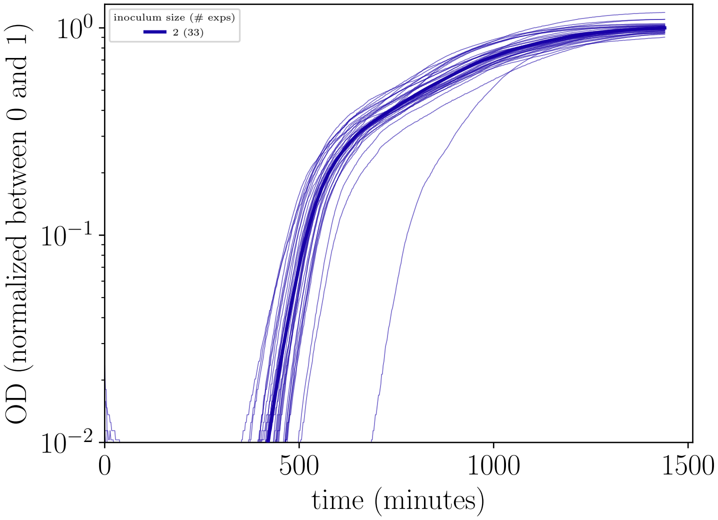
$$P_{ij}(t) = \int_0^t P_{jj}(t')\tau_{ij}(t-t')\mathrm{d}t'.$$

For large j, $\tau_{ij}(t) \approx P_{ij}(t)$.

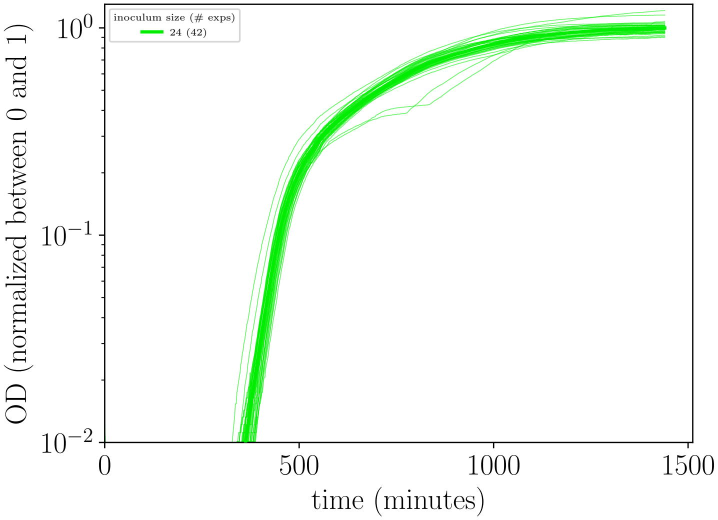
New experimental data



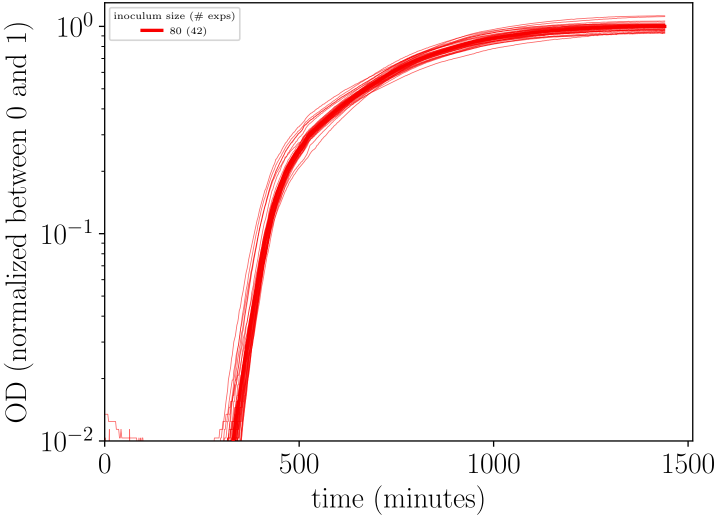
New experimental data



New experimental data

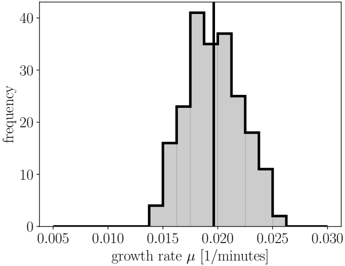


New experimental data

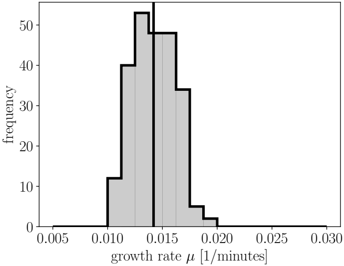


Growth rates across two different experiments

Growth rates are collected from every replicate and from every inoculum size



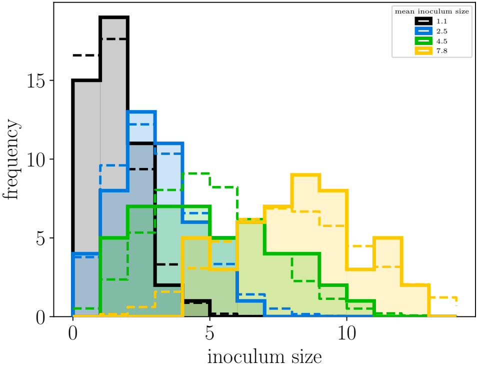
experiment 3



experiment 4 (aerobic growth)

Poisson noise

In our experiments, each replicate is inoculated by a micropipette containing some small volume of a solution extracted from a dilute mixture of *E. coli*, leading to Poisson distributed inoculum sizes.



Modeling Poisson noise

The distribution of inoculum sizes follows a Poisson distribution: for an average inoculum size i, the probability that a replicate's inoculum size is k is

$$\frac{e^{-i} i^k}{k!}.$$

If the growth dynamics following inoculation are deterministic, $P_{ij}^{\text{Pois,det}}(t)$ is simply the probability of drawing the "rewound" state $je^{-\mu t}$ from the inoculum's Poisson distribution:

$$P_{ij}^{\text{Pois,det}}(t) = \frac{e^{-i} i^{je^{-\mu t}}}{je^{-\mu t}}.$$

Modeling Poisson and intrinsic noise

The solution to the simple birth process (delta function inoculation, intrinsic noise) is

$$P_{ij}(t) = \frac{\mu(i+j-1)!}{(i-1)!(j-1)!} e^{-it\mu}(1-e^{-\mu t})^{j-1}.$$

If the inoculum size is Poisson distributed, the resulting solution will simply become

$$P_{ij}^{\mathrm{Pois}}(t) = \sum_{k=1}^{\infty} \frac{\mathrm{Pois}(k;i)}{1-\mathrm{Pois}(0;i)} P_{kj}(t) = \sum_{k=1}^{\infty} \frac{e^{-i} i^k}{k!(1-e^{-i})} P_{kj}(t)$$

Temporal spread of replicate trajectories

We are interested in the temporal spread of replicate trajectories $\mathrm{SD}(\tau_{ij}(t))$, evaluated at a large j (~ 10000). Specifically,

$$\langle \tau_{ij}(t) \rangle = \int_0^\infty \mathrm{d}t \, t \, \tau_{ij}(t),$$

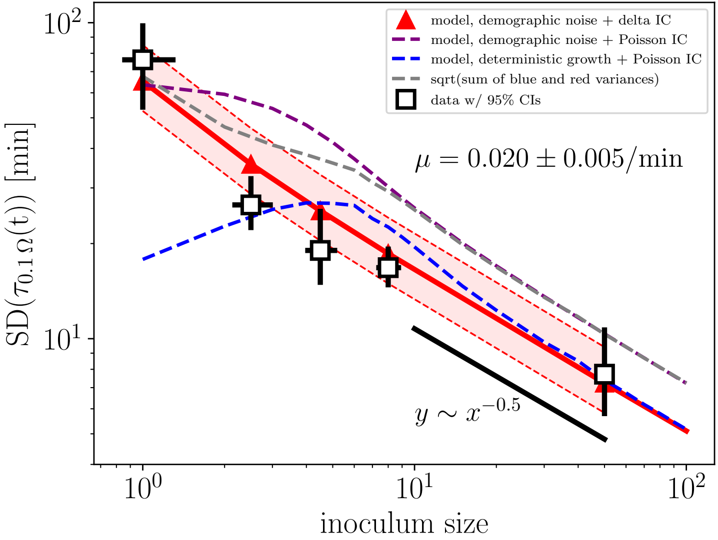
$$\sigma^2(\tau_{ij}(t)) = \int_0^\infty \mathrm{d}t \, (t - \langle \tau_{ij}(t) \rangle)^2 \, \tau_{ij}(t),$$

and

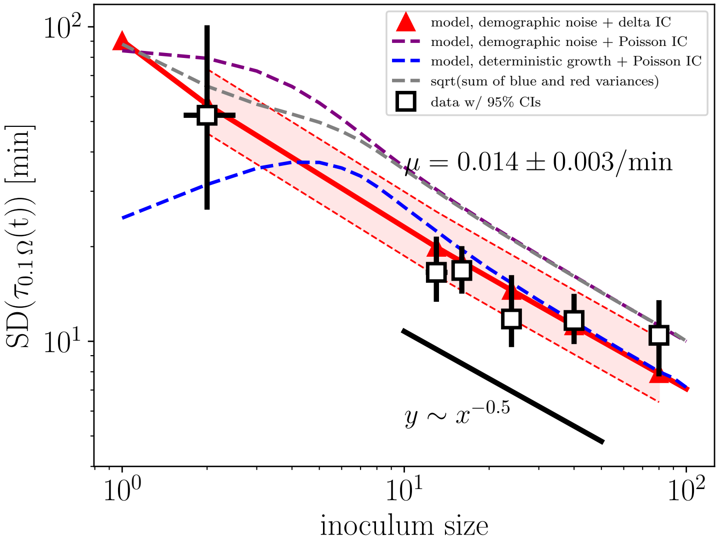
$$\mathrm{SD}(\tau_{ij}(t) = \sqrt{\sigma^2(\tau_{ij}(t))}.$$

This quantity can be calculated analytically for $P_{ij}(t)$, and numerically for $P_{ij}^{\mathrm{Pois}}(t)$ and $P_{ij}^{\mathrm{Pois,det}}(t)$.

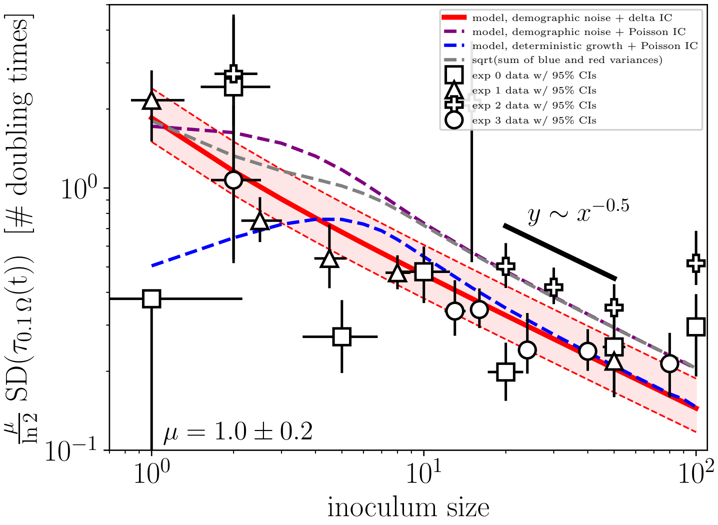
Previous experiment (5/15/22)



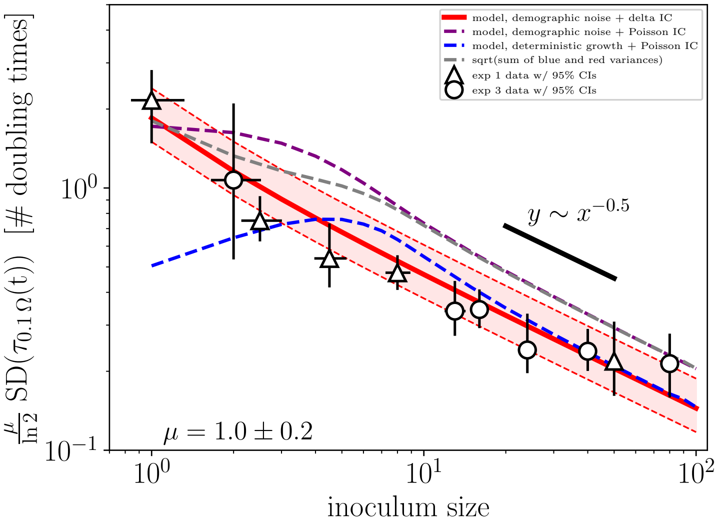
Recent experiment (5/31/22)



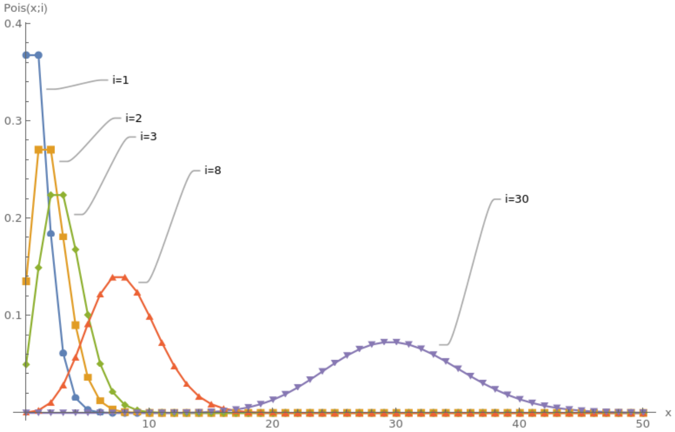
All experiments together



“Good” experiments together



Why does deterministic growth from Poisson IC have max effect at inoculum size ∼5?



strength of noise ∼ # doublings between low and high ends of distribution

Calculating π with bacteria

The standard deviation of the temporal spread in trajectories originating from a single individual is

$$\mathrm{SD}(\tau_{1,\infty}(t)) = \frac{\pi}{\sqrt{6}\mu}.$$

Our measured values:
$\mathrm{SD}(\tau_{1,\infty}(t)) = 75$ minutes
$\mu = 0.014$ / minute

$$\implies \pi = 2.6$$

(big if true)