Intrinsic variability in exponentially growing systems

June 3, 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

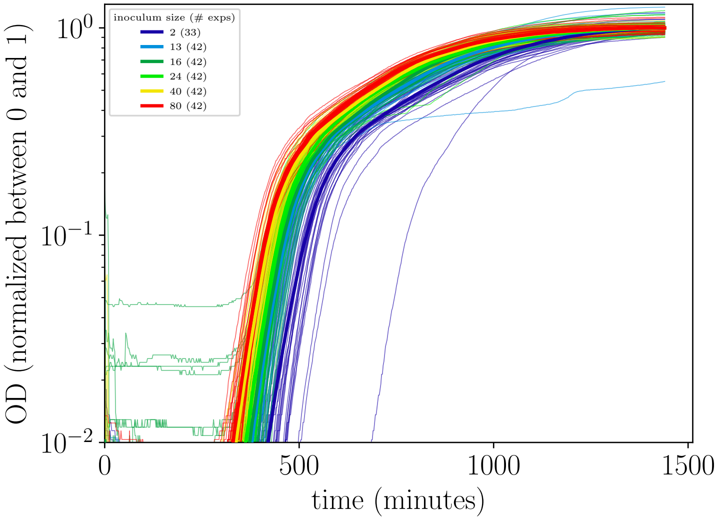
$$P_{jj}(t) = \mu j\, e^{\mu j t}.$$

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



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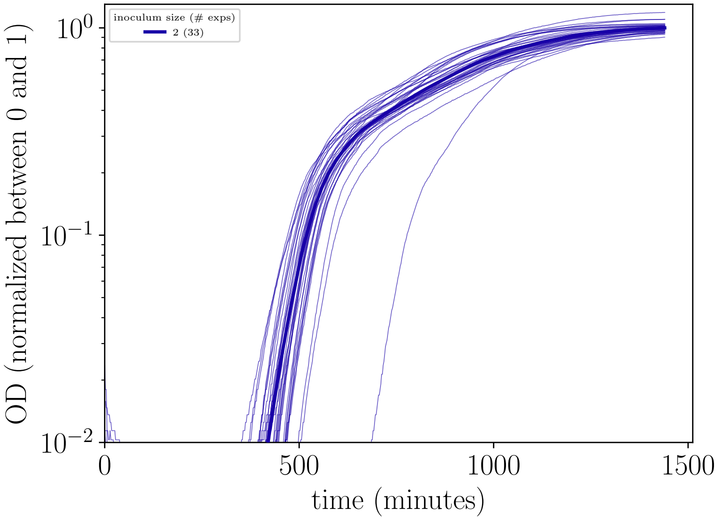

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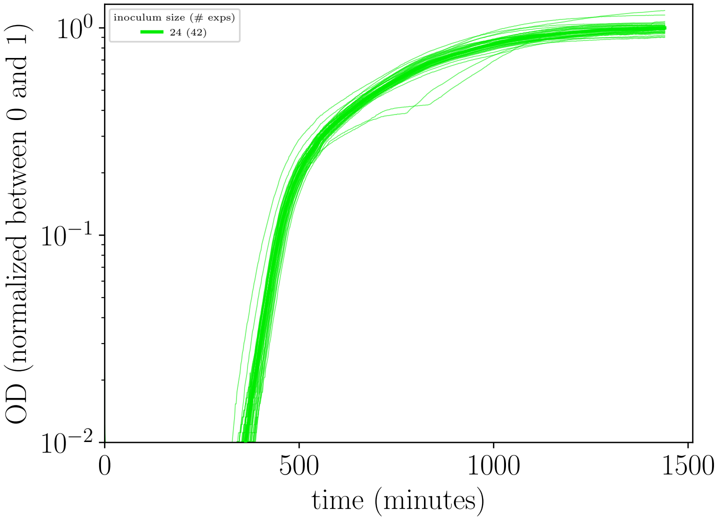
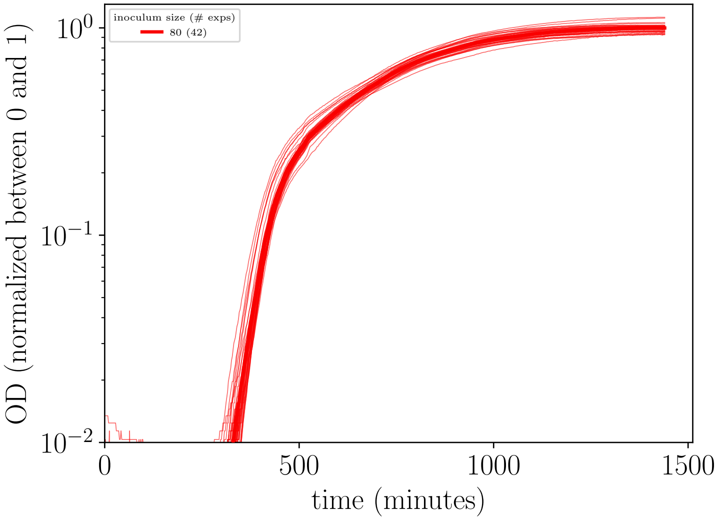
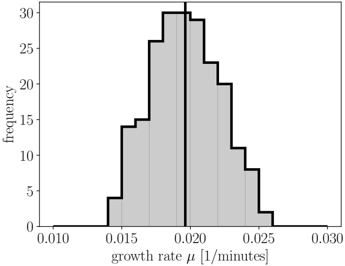


New experimental data

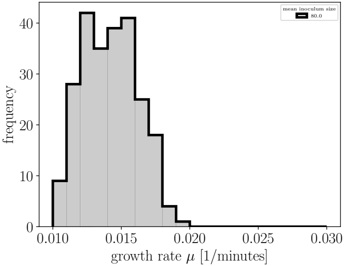


Growth rates across two different experiments

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



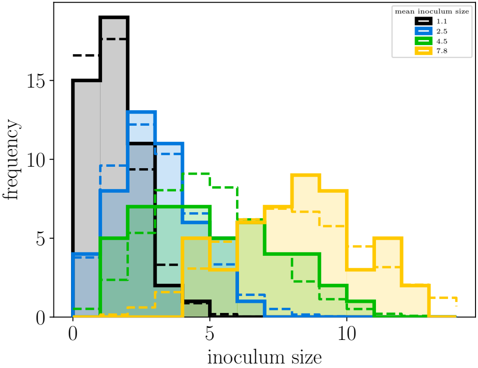
experiment 3



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

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

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,

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

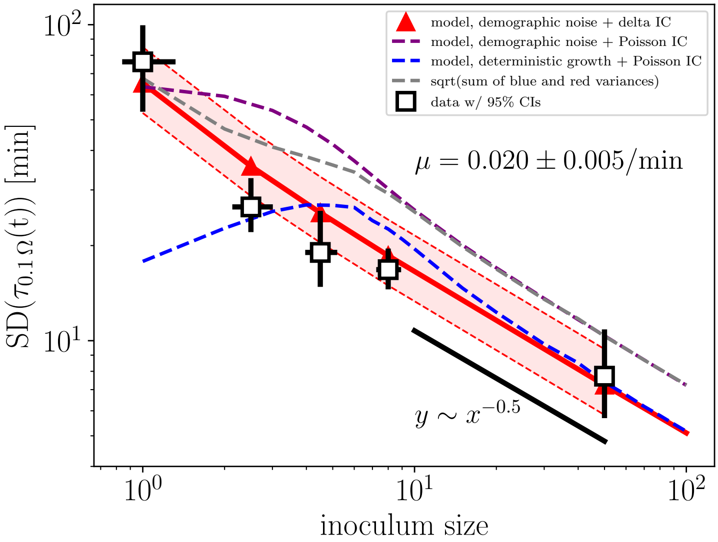
$$\sigma^2(\tau_{ij}(t)) = \int_0^\infty \mathrm{d}t \, (t - \langle \tau_{ij}(t) \rangle)^2 \, \tau_{ij}(t),$$

and

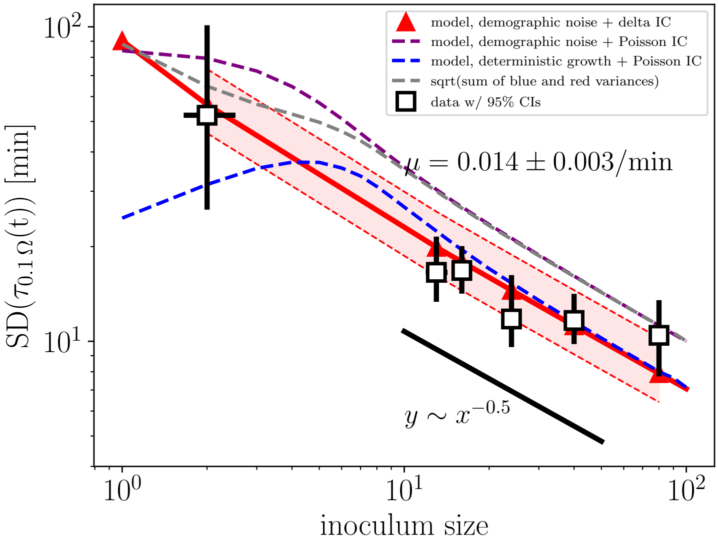
$$\mathrm{SD}(\tau_{ij}(t) = \sqrt{\sigma^2(\tau_{ij}(t))}.$$

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

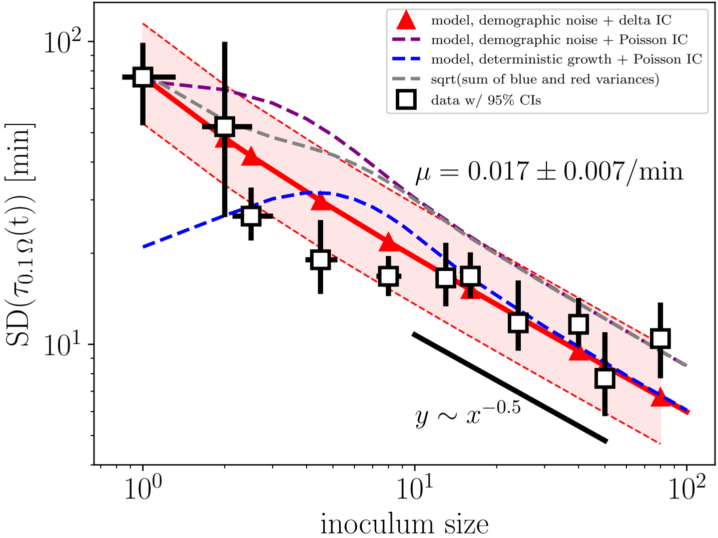
Previous experiment (5/15/22)



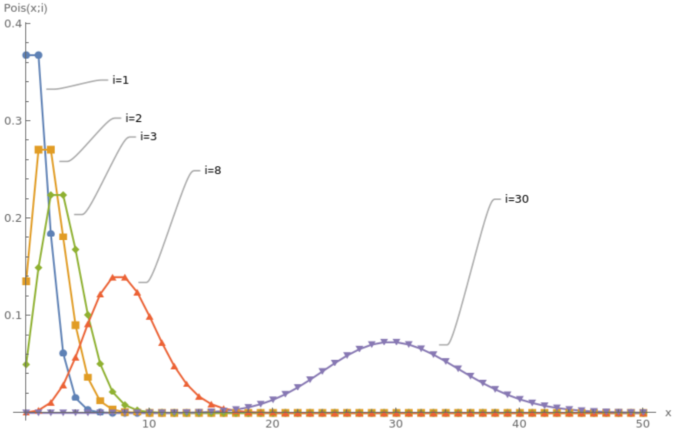
Recent experiment (5/31/22)



Both experiments together (but different μ!)



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

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

Our measured values:

$\mathsf{SD}(\tau_{1,\infty}(t)) = 75$ minutes
$\mu = 0.014$ / minute

$$\implies \pi = 2.6$$

(big if true)