Stochastic modeling of Pseudomonas syringae

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Introduction

- Biological Background:
  - A mixture of Pseudoomonas syringae (often called P. syringae in paper) was sprayed onto 14 day old bean plants. The bacteria can be potentially harmful to plants as seen in figure 1. Part of the initial study was to better understand the growth of this bacteria on crop plants. This pathogen has been studied since the 1900's and can ruin many plants such as: tomatoes, olives and bean plants.

Introduction

- Math Background
  - As the author quite plainly states, and with many mathematical modeling projects, "The aim of this work is to use a mathematical model to help understand(sic) the mechanisms" with in this case the mechanisms being growth of P. syringae on a leaf.
  - Many other papers have been written on aggregates and cover a variety of different topics, from aggregates to social situations. One quite well known example would be “From Individuals to Aggregations: the Interplay between Behavior and Physics” which studies and looks at a variety of aggregates on both micro and macro scale. See figure 2 for bluefin tuna school aggregate example.

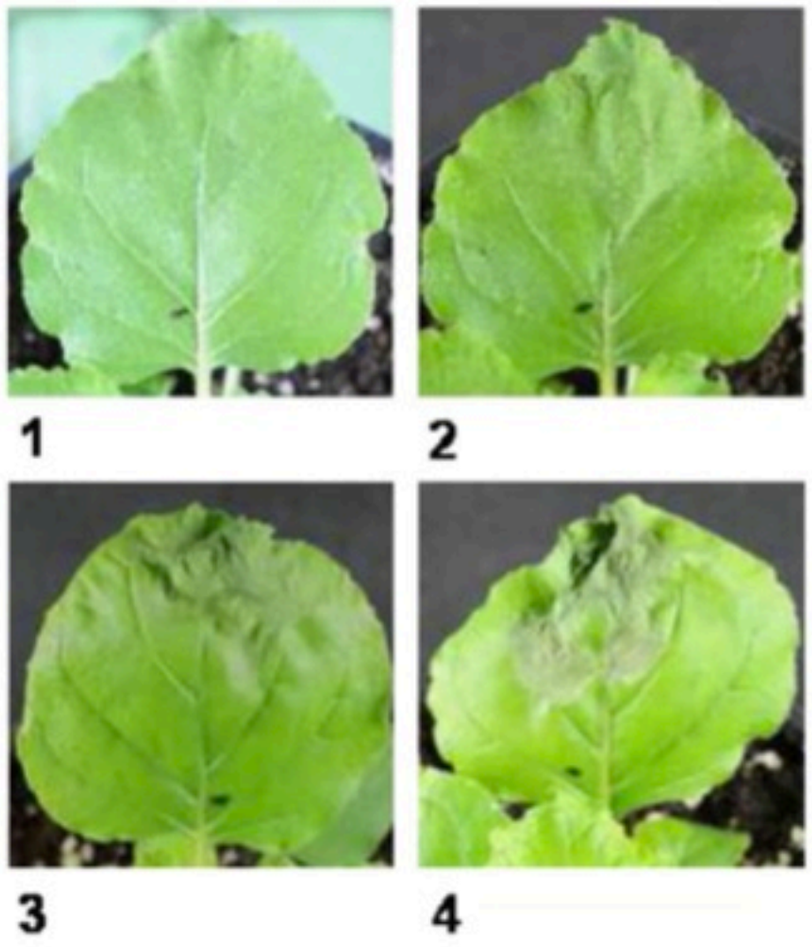


Fig. 2. Bacterial lesions caused by *Pseudomonas syringae* pv. syringae B728a in *N. benthamiana*, picture provided by Dr. Corina Vlot's group (Inducible resistance signalling), Institute of Biochemical Plant Pathology, Helmholtz Zentrum München. Pictures display the damage to the leaf in a period of 4 days. Reproduced with permission.

Figure 1 showing leaf damage.

Bluefin Tuna School's and Simulated Schools

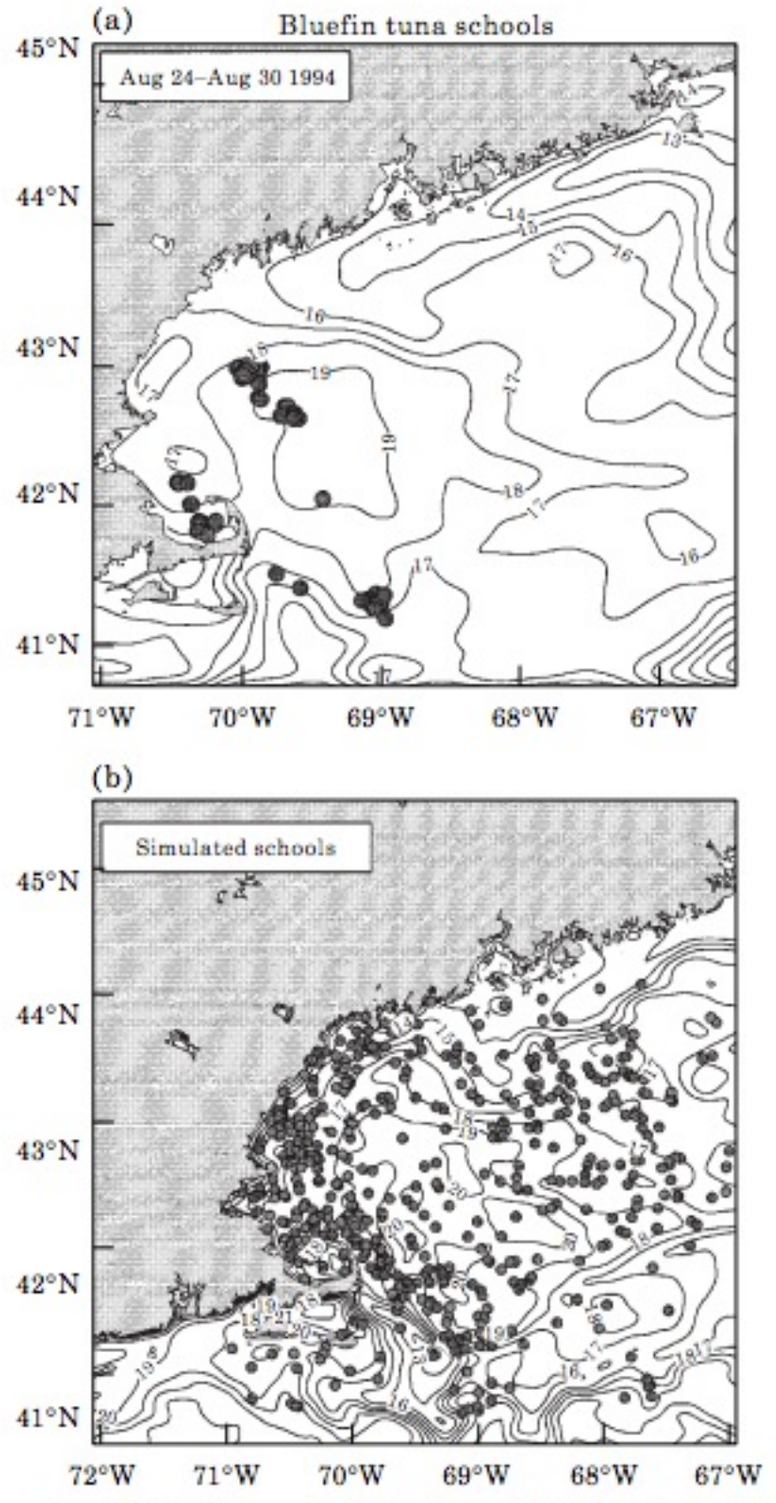


FIG. 13. (a) Observed distribution of bluefin schools. (b) Simulation using kinesis model.

Papers Motivation

- After looking around at other examples of bacterial growth, many authors may chose to use a probability distribution to model the data

- This article is aimed at understanding how it would arrive at such a distribution as to understand the growth of the bacteria. Authors state: "Rather than fitting a distribution to the experimental data, we have opted for a dynamic approach that may allow us to elucidate the mechanisms that generate the observed behavior by Dulla and Lindow"

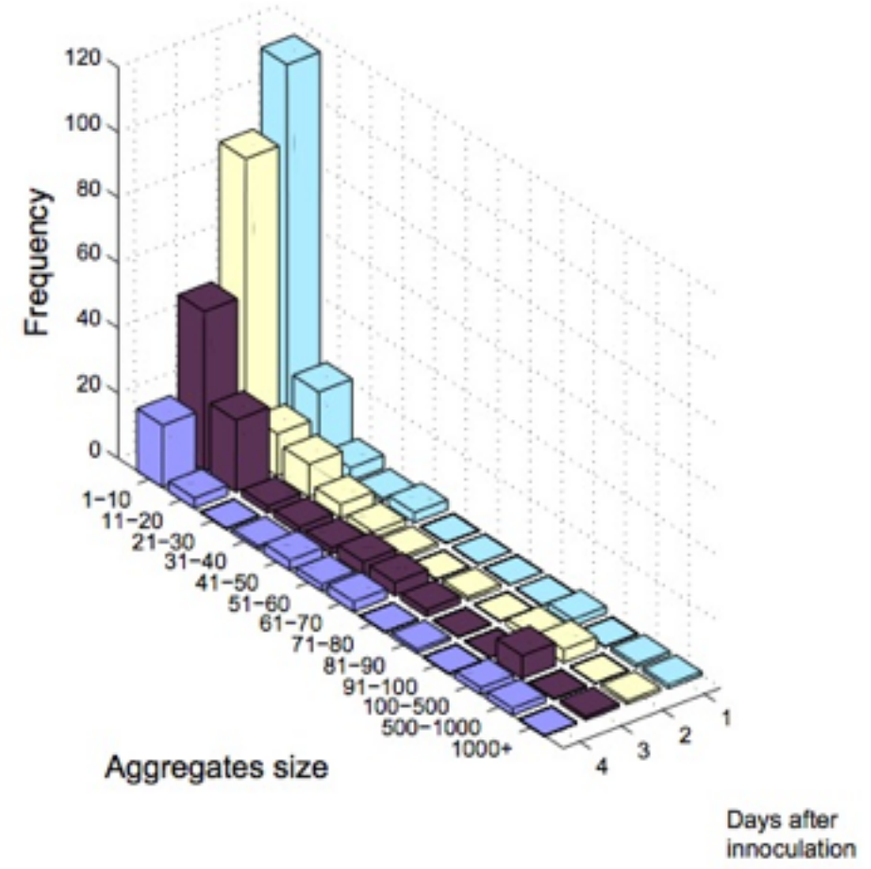


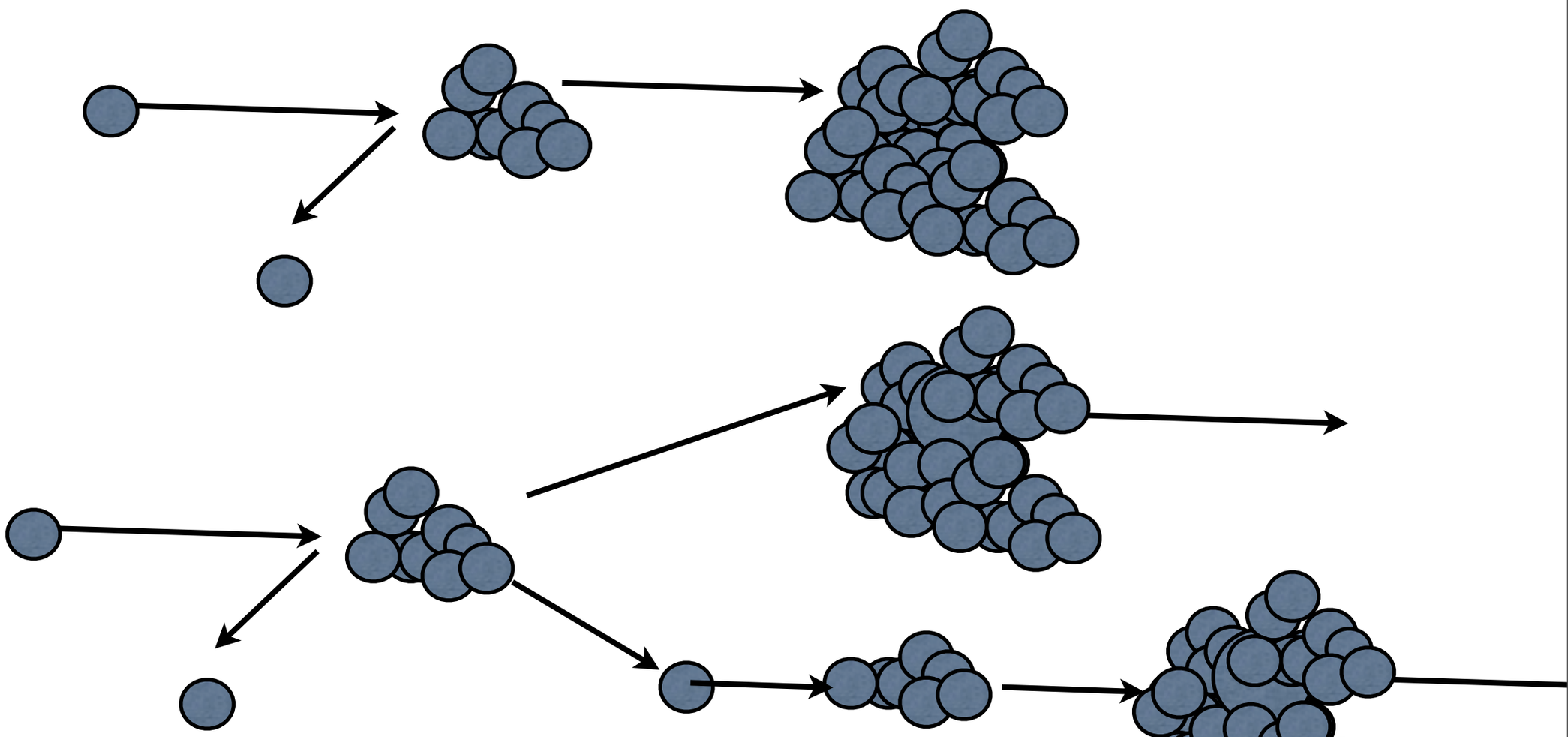
Fig. 3. Frequency distribution of bacterial aggregates on leaf surfaces following inoculation with *P. syringae* pv. syringae strain B728a. Experimental data from Dulla and Lindow [7].

Stochastic Model

- The model they choose is Stochastic, they do not even discuss deterministic
- Since all aggregates grow differently and independently, high degree of stochasticity
- Cannot say a cell will divide within a set amount of time for certain, only that it has a certain probability of doing so.

Mathematical Model

- This model consists of three basic parts, the logistic birth-death process, the carrying capacity and the migration rate.



Definitions

- Carrying capacity - the maximum colony size of each X_i colony. The carrying capacity was previously experimentally determined to be approximately the log-normal distribution. Carrying capacity was randomly taken from Matlab with lognrnd(2.71,1.78).
- Phyllosphere - the leaf surface or where the bacteria is inhabiting on the leaf
- Aggregate - more than 1 cell colony
- Monte Carlo Simulation - “computer algorithms that use random sampling to obtain numerical results”

Assumptions

- Colony migration (new colonies) do not affect old colonies
- Cells can at any point migrate
- Cells leave one by one for migration
- Colonies do no not effect one another, therefore each colony simulated independently
- Two sources of new colonies are Inoculation(only initial) and Migration
- N(t) at t=0, N(0) = 1
- Sampling from lognormal distribution is unbiased. (Carrying Capacity has potential to be very very large even though experimentally this is impossible)

Parameters

- α - growth/birth rate (.4)
- δ - death rate (.1)
- I - migration
- μ - lognormal parameter
- σ - lognormal parameter
- K - carrying capacity
- $N(t)$ - the number of colonies that were formed until time t
- $X_i(t)$ - the number of cells in each colony
- λ_i - birth rate, defined as $\lambda_i = i\lambda(1 - \frac{i}{K})$
- δ_i - death rate, defined as $\delta_i = i\delta$

Equations

- $X(t)$ is a markov stochastic process with state spaces S = 0,1,...,K. i.e. memoryless with max population size K (integer step sizes)
- $Pr\{X(t+\Delta t) = j+1 | X(t) = j\} = \lambda_j \Delta t$ - birth
- $Pr\{X(t+\Delta t) = j-1 | X(t) = j\} = \delta_j \Delta t$ - death
- $Pr\{X(t+\Delta t) = k | X(t) = j\} = 0$ as $\Delta t \to 0$

Transition Probabilities Satisfy:

- $\dot{p}_x^{X_i}(t) = p_{x-1}^{X_i}(t)\lambda_{i,x-1} + (\delta(x+1)+I)p_{x+1}^{X_i} - (\lambda_x + \delta x + I)p_x^{X_i}(t)$
- $\dot{p}_m^N(t) = p_{m-1}^N(t)(m-1)I - p_m^N(t)mI$

Solutions to this above equation can be obtained recursively and result in:

- $p_n^N(t) = e^{-It}(1-e^{-It})^{n-1}$

- Colony Formation Time: $T_i = min\{t \le 0; N(t) \le i\}$
- $X_i(t) = Y_i(t - T_i)$ if $t > T_i$, but 0 if $t < T_i$
- Total Number of Colonies: $N(t) = 1 + \sum_{i=1}^{\infty} N_i(t - T_i)$
- Y_i is birth-death process with $Y_i(0) = 1$ initial population always 1
- The birth or growth rate, is: $\lambda_{i,x}$, where $\lambda_{x,i} = x\lambda(1 - \frac{x}{K_i})$
  since K_i is the carrying capacity for colony i, and x is colony size, as x → K, growth or birth rate λ_i goes to 0. This allows for the colony size to asymptotically reach some carrying capacity K, as shown in later picture.

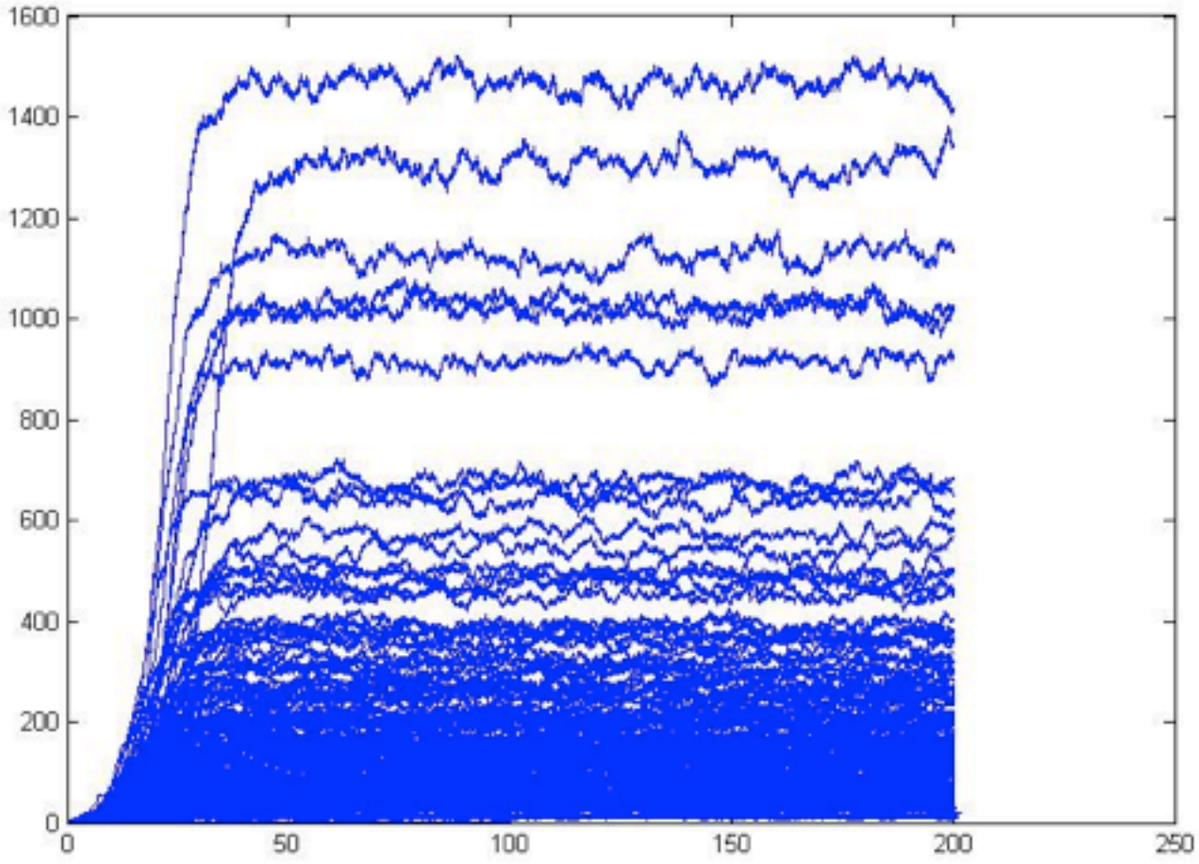
Papers Simulation Results

- The model was able to reflect the results achieved in the original experiment and is therefore useful for studying the mechanisms behind this pathogen and other similar ones.

- The model reflects some interesting results such as, although the majority of colonies are in sizes less than 100, the majority of the populations is in colonies greater than 100.

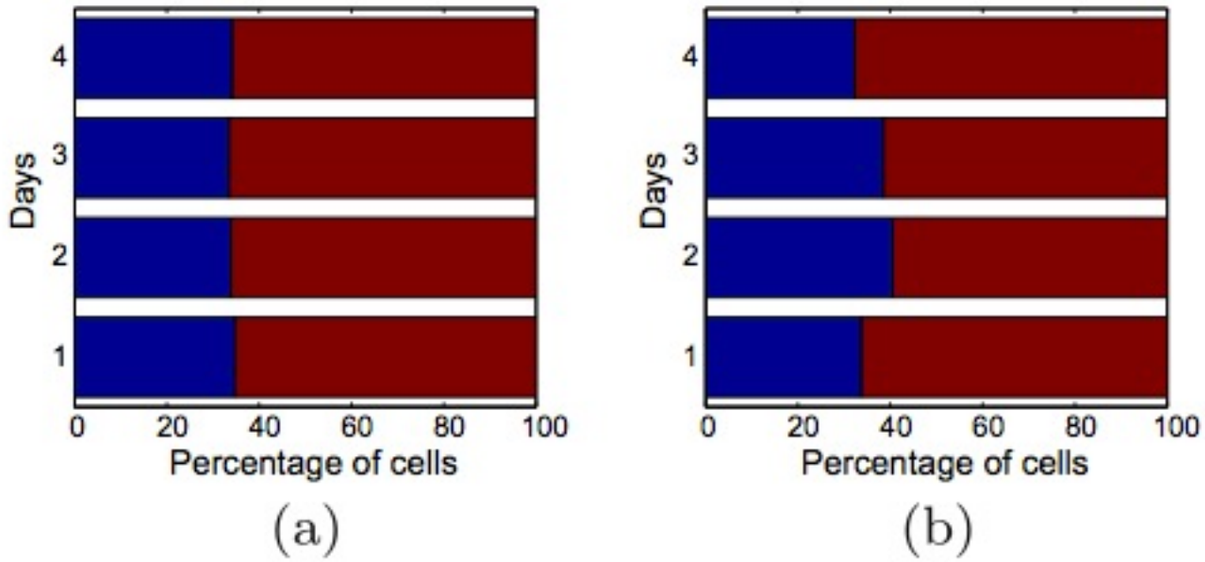
- Meaning lots of population in a few aggregates.

- Believe they used integer values for carrying capacity



Simulations vs Experimental

- In both experimental and simulation results:
  - Strong right-hand-skewed frequency distribution.
  - Large aggregates not frequent but account for majority of cells (more than 50% in colonies larger than 100)
  - Majority of colonies are small



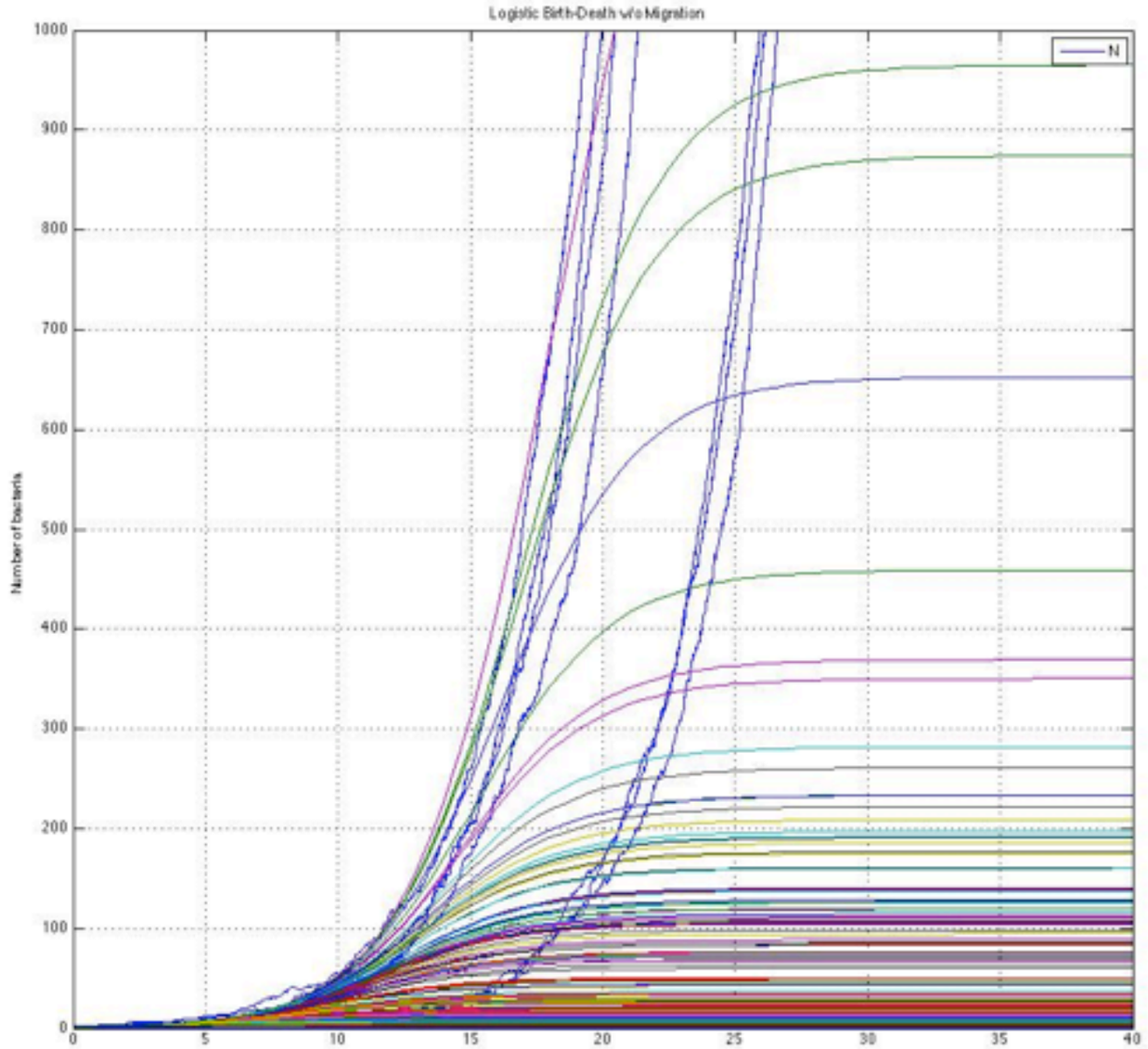
Percentage of cells smaller than 100 (blue) and larger than 100 (red) with simulation results on left and experimental results on right.

My Initial Results

- Simbiology: Since stochastic solver ONLY works with Mass Action law (i.e. user defined kinetic laws will not work with 'ssa'), and Mas Action law's cannot seemingly have a carrying capacity, not viable option?

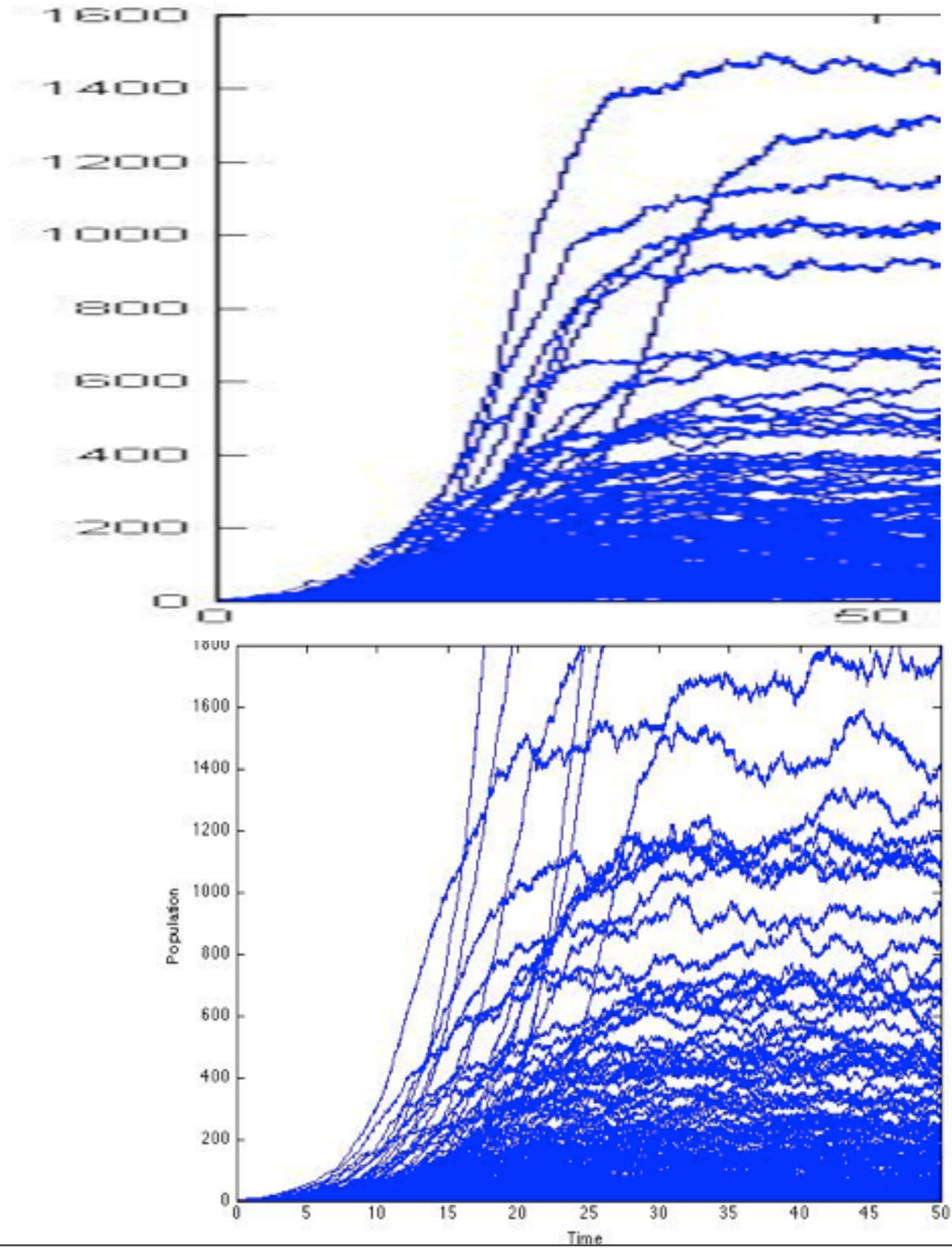
- Contacted the J. Perez-Velazquez, who told me the entire simulation was carried out in Matlab

- Created deterministic results in Matlab with carry capacity. Results were similar but not identical to articles simulation but stochastic will inherently be different that stochastic process.



Second Results

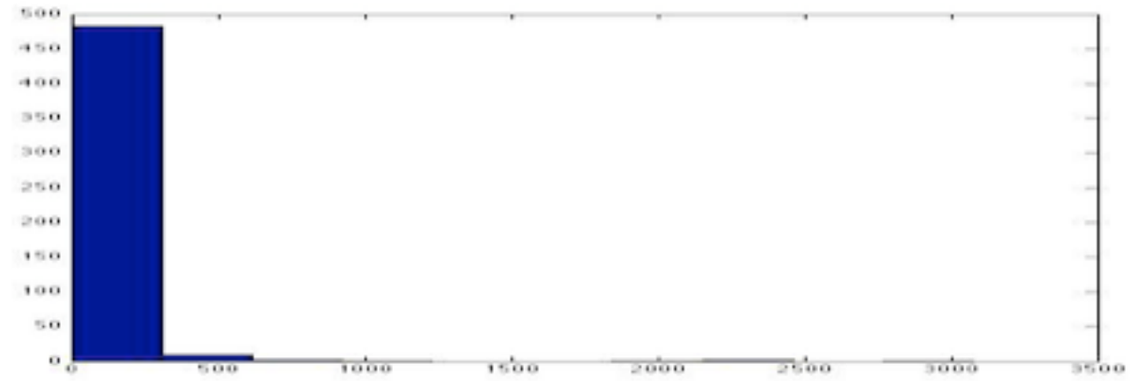
- Able to reproduce results with Simbiology and Migration = 0
- Much quicker than experimenter in getting to carrying capacity
- Sampling from lognorm was much wider in mine

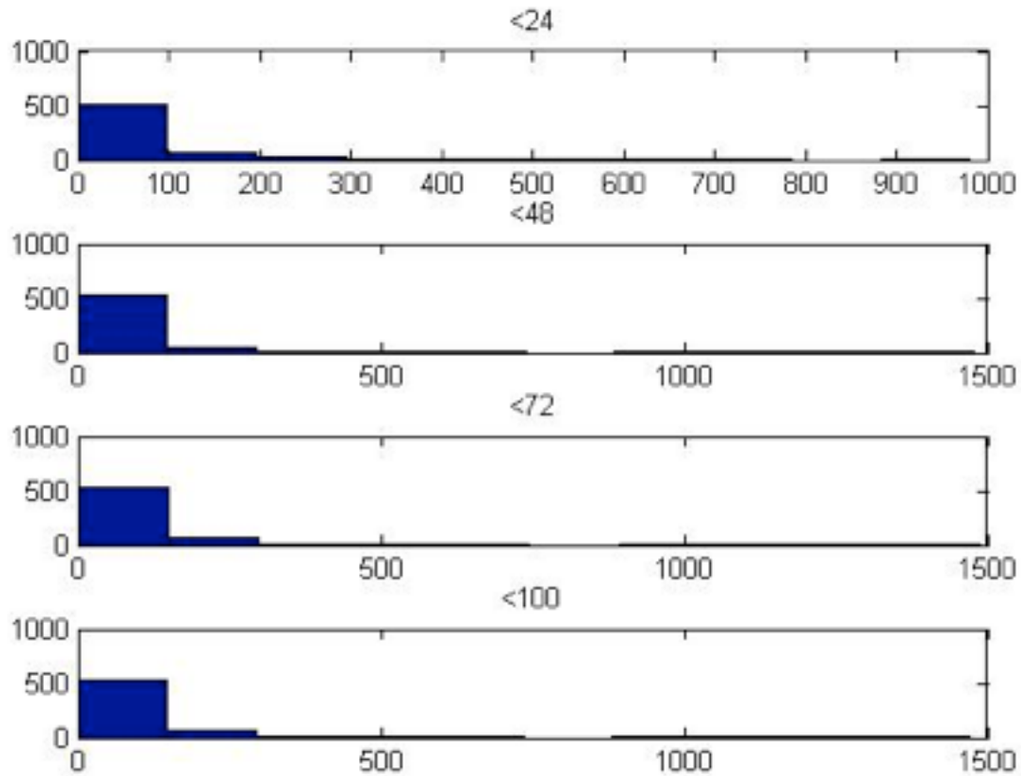


Histogram Comparison

- Histogram is similar for first 24 hours, but not identical even when their migration was 0 (i.e. no new colonies).

- Believe this was because their sampling was much higher and stochastic: more chance of variation and more colonies with low aggregates.





Paper Continued Simulation

- Paper went on to further simulate results such as varying leaf surface environment (by varying lognormal parameters)

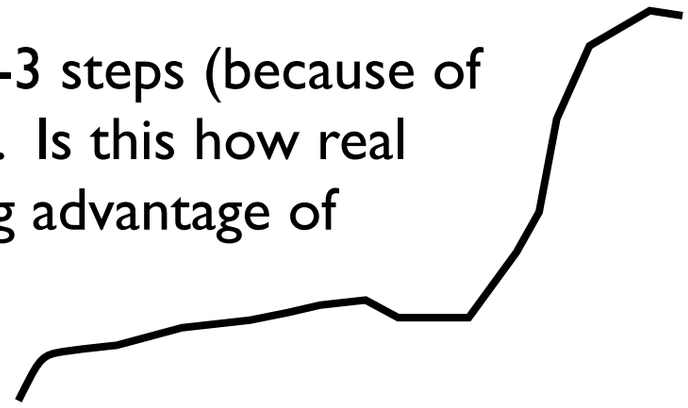
- Discussed how simulation matched one experimental data set more than another and how experiments were carried out varied cell migration

- Varied migration rate, from initial I=0 (no migration) to I=1 (high migration)
    - When migration is 0, small colonies will decrease with time.
    - Migration has greatest affect on small colonies.
- Two questions in end:
    - Effect of varying rate of migration
    - Effect of large migrations

Suggestions For Model

- While the model went on to further study "Starvation driven migration", in which migration only occurred in colonies with greater than 50 cells to (so that only colonies with presumably fewer nutrients available would cause migration), an interesting model would be to compute it so that migration can happen at all times but becomes much more frequent close to carrying capacity.

- For the most part, cell colonies either died within first 2-3 steps (because of stochasticity) or reached carrying capacity and stabilized. Is this how real plant colonies occur or is there more fluctuation? (taking advantage of susceptibility in plant)



- Step size was in 1 hour increments, further options?

Conclusion

- Without a carrying capacity, the results are useless since cell colonies will grow exponentially.

- Deterministic results quite similar to stochastic results but deterministic results arrive at carrying capacity slower.

- Global and local effects affect population dynamics.

- Population process that resembles experimental data was successful.

- Possible aim of model is for minimizing pathogens onset.