



# Modeling Microbial Growth and Resistance

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Data+ 2021

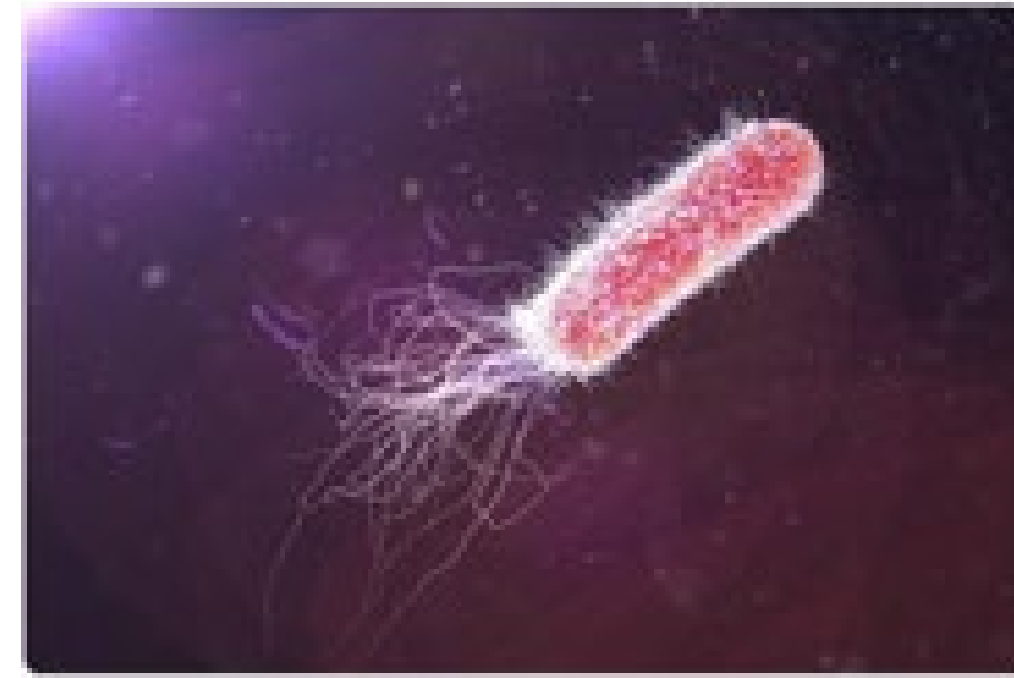


## Microbiology

- **Growth data**
  - Collected from optical density
  - Traditionally creates s-shaped curves
  - Treating infections, food safety, genomics, etc.
- **Non-standard growth under stress**
  - Extremophiles
  - Deleterious mutations

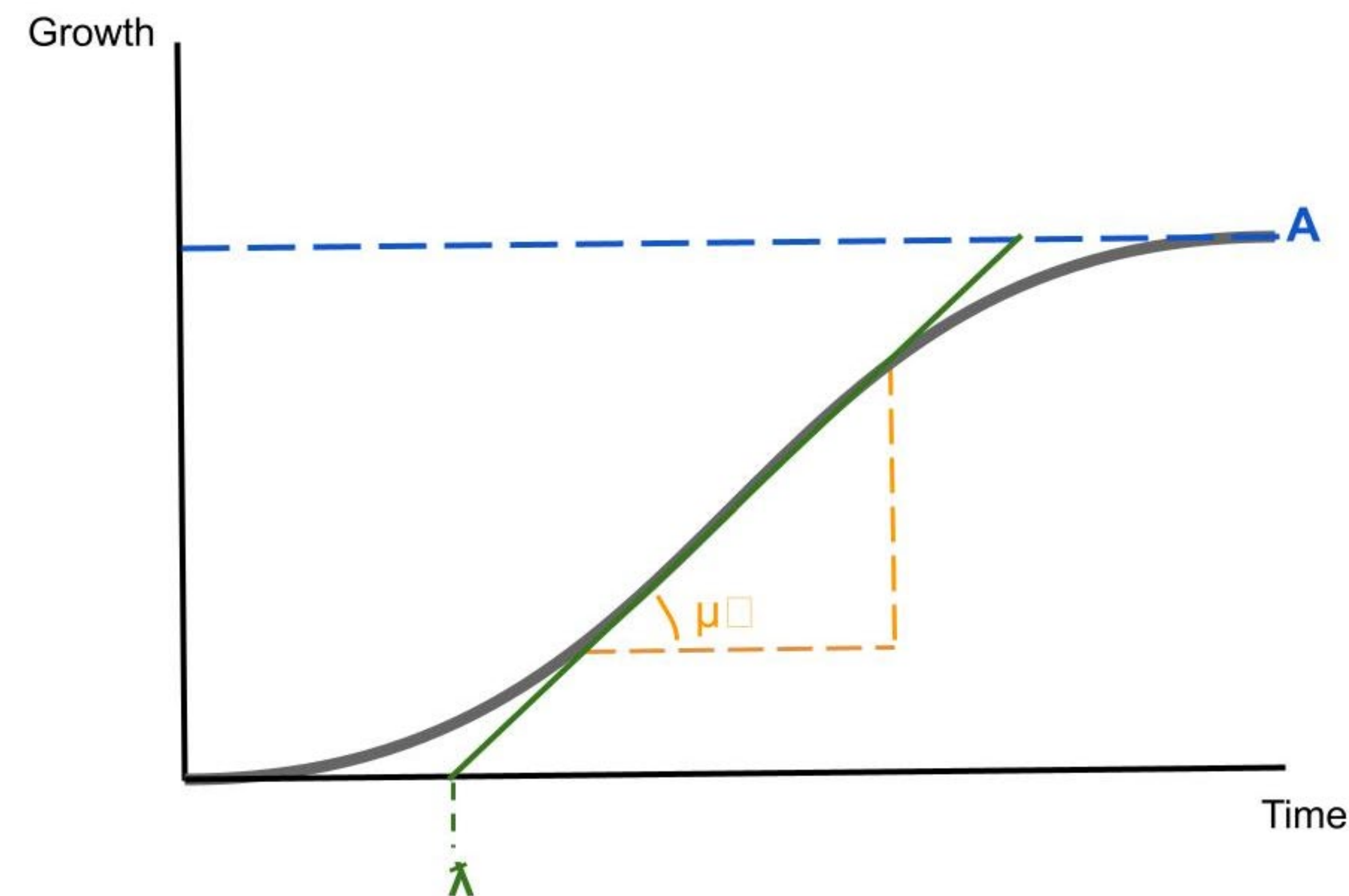


Baseline Strain



Genetically Altered Strain

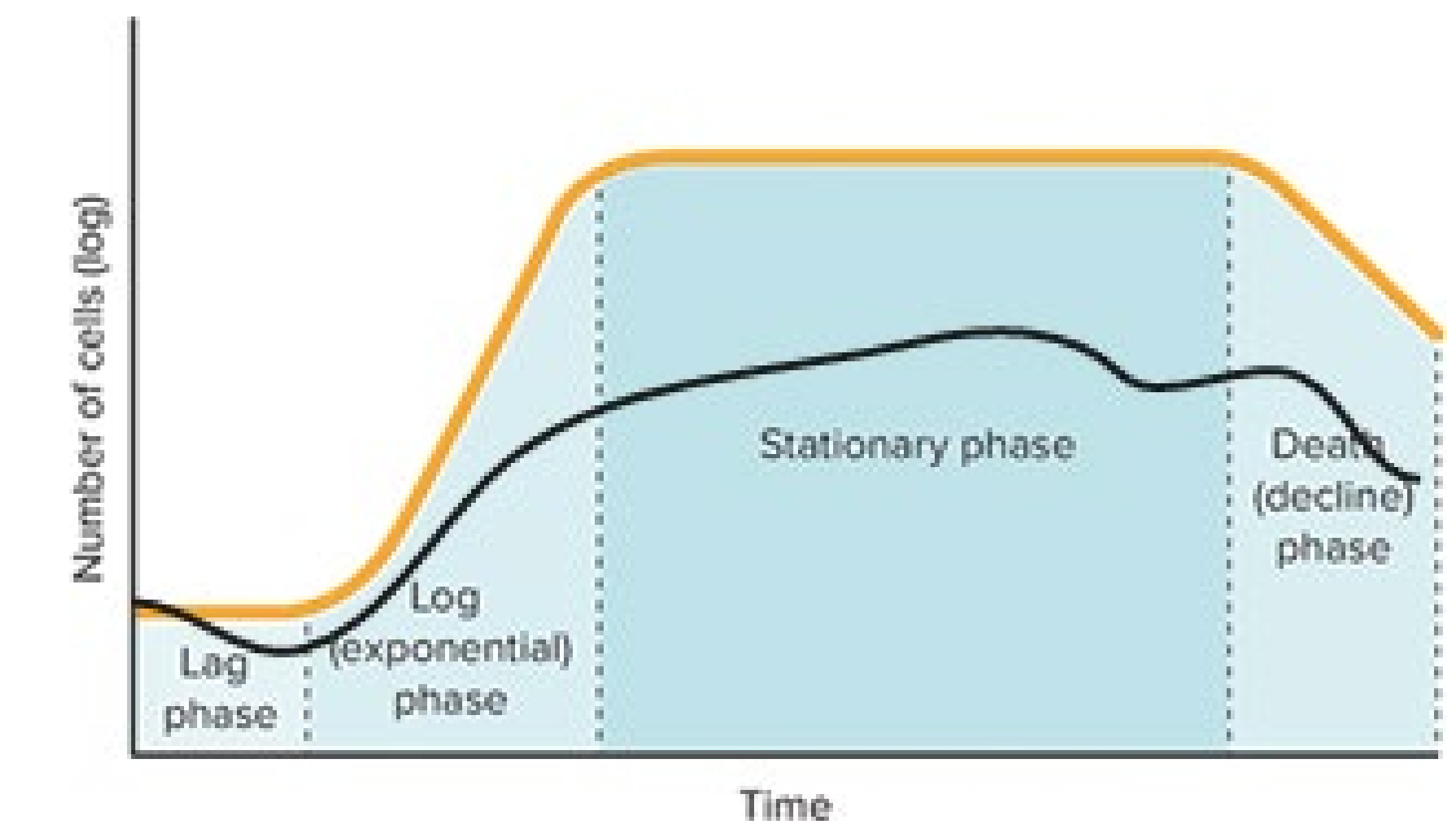
## Standard Parametric Models



~ Asymptote ~ Lagtime ~ Maximum Specific Growth Rate

## What is Phenom?

- **Phenom ~ a Hierarchical Gaussian Process Model**
  - Non-parametric
  - > allows departure from standard 's' curves
  - Mixed Effects Model
    - Accounts for batch effects
    - Accounts for replicate effects



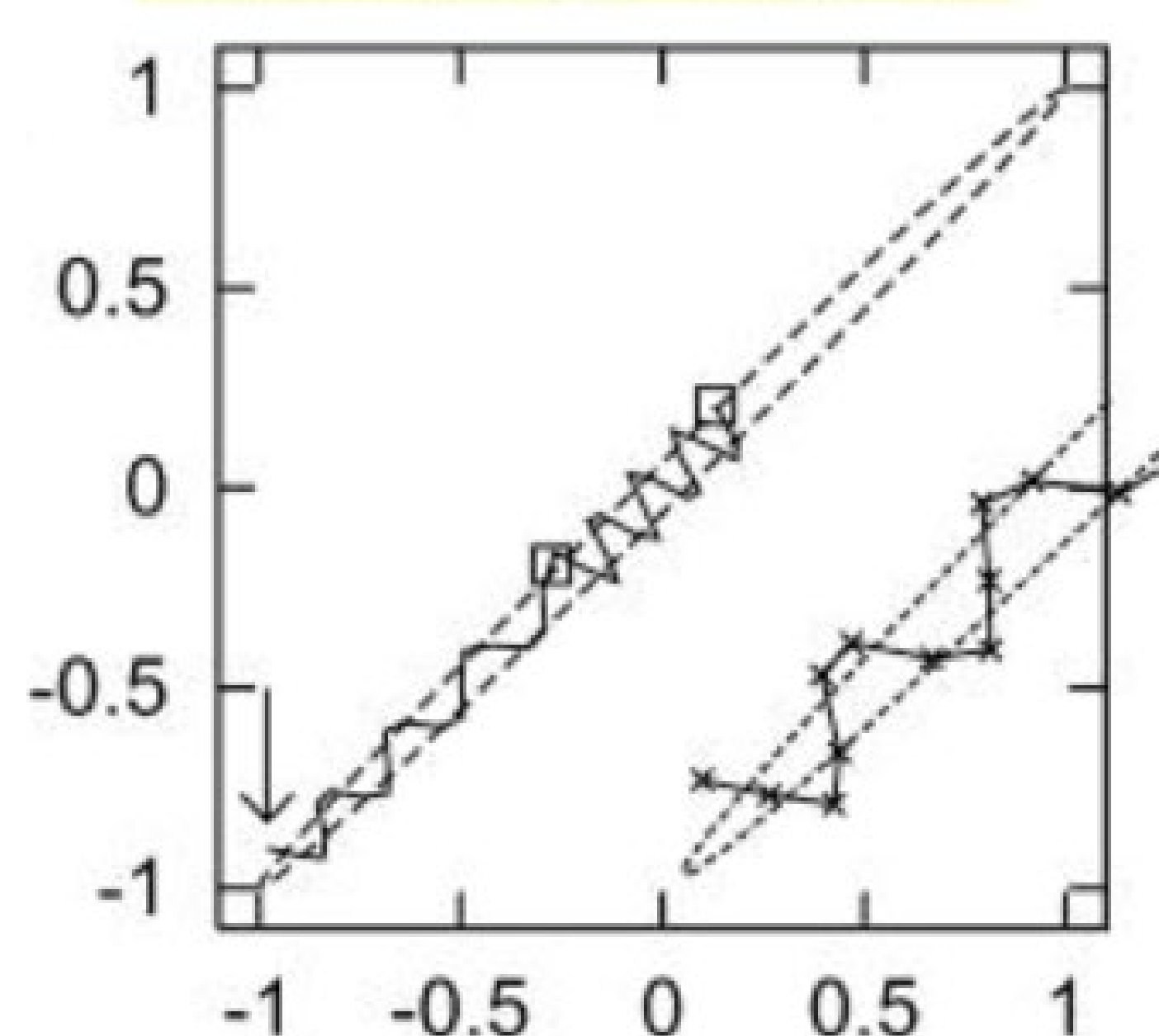
## Methodology

- **Gaussian Process Regression**
- **Markov Chain Monte Carlo**
- **Solve for:  $\lambda, \alpha, \sigma, f^*$** 
  - Assign priors to the unknowns, then use MCMC to create posterior inferences

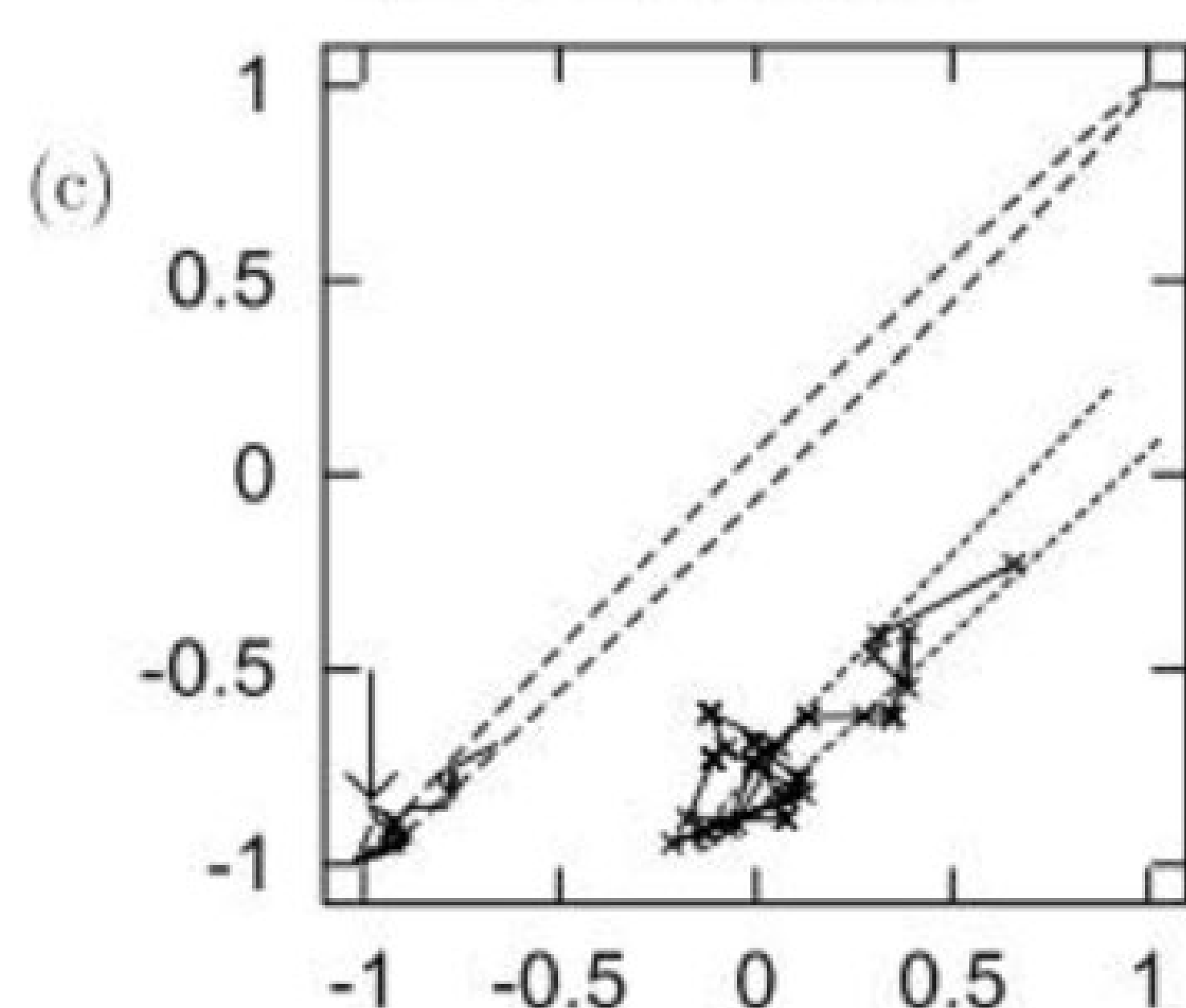
$$y_r(t) = \begin{cases} m(t) + \epsilon_r(t) & \text{if standard growth} \\ m(t) + \delta(t) + \epsilon_r(t) & \text{otherwise} \end{cases}$$

$$f(t) \sim GP(\hat{f}(t), \kappa(t, t'))$$

Hamiltonian Monte Carlo

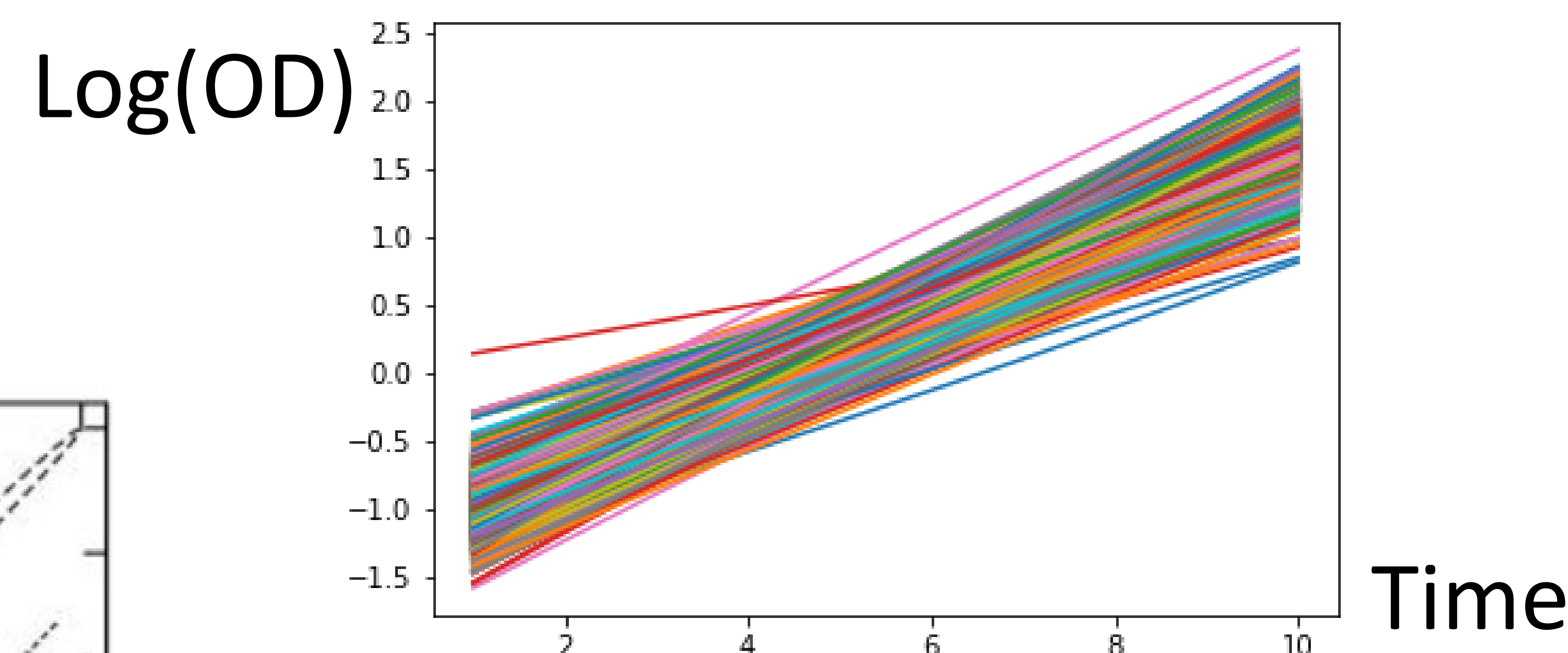


Simple Metropolis



## Our Results

- **Selection of treatment variables from metadata**
  - Formula terms for each variable and their interactions
- **Compiled stan models, samples from MCMC chains, MCMC diagnostic tests**
- **Technological procedure**
  - Compatible pystan environment
  - Package requirements, C++ compiler



Inference for Stan model: anon\_model\_cdb9efd1561f4a500f3bd7aff9cfed85.  
 2 chains, each with iter=2000; warmup=1000; thin=1;  
 post-warmup draws per chain=1000, total post-warmup draws=2000.

	mean	se_mean	sd	2.5%	25%	50%	75%	97.5%	n_eff	Rhat
lengthscale[1]	5.77	0.03	0.85	5.02	5.21	5.51	6.01	8.0	1135	1.0
lengthscale[2]	11.5	0.21	8.2	5.05	6.09	8.05	13.7	36.42	1460	1.0
alpha[1]	6.3	0.15	1.94	3.69	4.94	5.99	7.23	10.8	171	1.01
alpha[2]	0.79	0.04	0.62	0.13	0.36	0.59	1.03	2.43	218	1.0
sigma	0.42	3.6e-3	0.07	0.29	0.37	0.41	0.46	0.58	414	1.0
f_eta[1,1]	-0.22	2.9e-3	0.06	-0.34	-0.26	-0.22	-0.18	-0.12	409	1.0
f_eta[2,1]	0.65	0.03	0.45	0.06	0.3	0.57	0.93	1.69	315	1.0
f_eta[3,1]	-0.6	0.03	0.46	-1.67	-0.87	-0.54	-0.25	0.03	302	1.0
f_eta[1,2]	2.55	0.03	0.62	1.41	2.12	2.49	2.98	3.84	395	1.0
f_eta[2,2]	0.33	0.03	0.99	-1.66	-0.31	0.36	1.01	2.21	1040	1.0
f_eta[3,2]	-0.68	0.05	1.05	-2.67	-1.39	-0.7	0.06	1.35	417	1.0

## Next Steps: Deployment

- **Remote desktop vs web application**
- **Jupyterhub with Kubernetes**
  - On Google Cloud Kubernetes engine: node pools and servers
  - Utilize Docker to customize user environments
- **Alternatives: Django, Flask, CherryPy, other python web app platforms**

## Acknowledgments

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## Citations

- **Tonner PD, Darnell CL, Bushell FML, Lund PA, Schmid AK, et al. (2020) A Bayesian non-parametric mixed-effects model of microbial growth curves. PLOS Computational Biology 16(10): e1008366. <https://doi.org/10.1371/journal.pcbi.1008366>**
- **Wongkamthong, C., Patterson, A., and Krinke, J. (2021). A Graphical User Interface for Bayesian Microbial Growth Modeling. Retrieved from [https://gitlab.oit.duke.edu/mids-capstone-projects/2020-2021/phenom\\_gui](https://gitlab.oit.duke.edu/mids-capstone-projects/2020-2021/phenom_gui)**
- **Zweitereing, M. H., Jongenburger, I., Rombouts, F. M., and Van't Riet, K. (1990). Modeling of the Bacterial Growth Curve. Applied and Environmental Microbiology, 56(6)**