Lecture 2: Microbial growth fundamentals

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September 8, 2025

Minimal models of microbial growth

The principles of microbial growth are critical for building an understanding of microbial ecology, evolution, and physiology. We start by considering the simplest possible *reasonable* model of growth, where a population of n cells grows at a constant per-capita rate.

$$\frac{dn}{dt} = \lambda \cdot n \tag{1}$$

which means that the population is growing *exponentially* in time: $n(t) = n(0)e^{\lambda t}$. This is a useful model and one can often design experimental conditions that permit exponential growth to be observed. We note that this model is *phenomenological* in nature, meaning that we defined the parameter λ without attempting to investigate the underlying mechanisms that control the value of λ.

However, when we perform real experiments in flasks we do not observe exponential growth forever as predicted by the model. Instead, one finds that n tends to saturate over time, meaning that the $\frac{dn}{dt}$ continues to decrease towards zero. This saturation is because the formation of biomass requires resources (e.g., carbon). In a batch culture experiment resources are provided at the start of the experiment, meaning that their concentration decreases with time as microbes continue to grow. We will now use this experimental detail to derive a model of growth where n saturates over time.

We start with a system of ODEs where a microbial population of n cells consumes a single resource c to grow at rate $\lambda(c)$

$$\frac{dn}{dt} = r(c)n \tag{2a}$$

$$\frac{dc}{dt} = -\frac{\lambda(c)n}{Y} \tag{2b}$$

where Y represents the cell yield per-unit resource. Notice that we have set the growth rate so that it is now a *function* of c. This introduction is necessary, as otherwise the population would grow exponentially forever. You have now setup an example of what is known in the literature as *consumer-resource models*, a fundamental class of ecological models that has provided considerable insight into the dynamics and structure of communities [1, 2].

We now have to identify an appropriate function for the resource-dependent growth rate. One finds that the Monod function is usually sufficient for capturing the relationship between growth rate and resource concentration [3].

$$\lambda(c) = \lambda_{\max}\frac{c}{c+K} \tag{3}$$

where $\lambda_{\max}$ is the maximum possible rate of growth and K is the half-saturation constant where $r(c)/r_{\max} = \frac{1}{2}$. For those interested in the typical values of K in experimental data see [4]. The Monod function has the following limiting behavior (Fig. 1):

1. Linear rate of growth when $c \ll K \ \rightarrow \lambda(c) \approx \frac{\lambda_{\max}}{K}c$
2. Constant rate of growth (exponential) when $c \gg K \ \rightarrow \lambda \approx \lambda_{\max}$

We can then derive a form of the ODE $\frac{dn}{dt}$ that does **not** depend on the resource concentration by:

1. Assuming that the half-saturation constant is sufficiently large relative to the *initial* concentration of supplied resources ($K \gg c(0)$).
2. Using the principle of mass conservation.

This first assumption holds in a batch culture setting because the limiting resource decreases as a function of time. Under the principle of mass conservation, resources and yield-corrected abundances must sum to a constant total mass at any given time $B \equiv \frac{n(t)}{Y} + c(t)$. This constraint allows us to obtain a function for $c(t)$. We then obtain the following single differential equation

$$\frac{dn}{dt} = \frac{B\lambda_{\max}}{K}n\left(1 - \frac{n}{YB}\right) \tag{4a}$$

$$= \tilde{\lambda}\cdot n\left(1 - \frac{n}{\tilde{K}}\right) \tag{4b}$$

where we have defined our final effective parameters in terms of consumer-resource mechanisms: $\tilde{\lambda} \equiv \frac{B\lambda_{\max}}{K}$ and $\tilde{K} \equiv YB$. The solution to the above ODE with initial condition $n(0)$ is

$$\tilde{\lambda} dt = \frac{dn}{n\left(1 - \frac{n}{\tilde{K}}\right)} \tag{5a}$$

$$\tilde{\lambda} t = \int_{n(0)}^{n(t)} dn \left[\frac{1}{n} + \frac{1}{\tilde{K}} \frac{1}{1 - \frac{n}{\tilde{K}}}\right] \tag{5b}$$

$$= \ln\left(\frac{n}{1 - \frac{n}{\tilde{K}}}\right)\Bigg|_{n(0)}^{n(t)} \tag{5c}$$

$$\rightarrow n(t) = \frac{n(0)e^{\tilde{\lambda}t}}{1 + \frac{n(0)}{\tilde{K}}\left(e^{\tilde{\lambda}t} - 1\right)} \tag{5d}$$

This resulting model is known as the Verhulst model of **logistic growth**, and it reproduces the saturating behavior observed in real experiments (Fig. 1). Therefore, a model of logistic growth can be appropriate for microbial microcosm experiments under certain conditions. For instance, the half-saturation constant must be sufficiently large relative to the supplied concentration of resources, a requirement that can, in principle, be manipulated by the experimenter (you). It is also necessary to consider properties of growth that we did not include in the model that would change its qualitative behavior (e.g., death).

A minimal model of enzyme kinetics

Resources are ultimately converted to biomass through biochemical reactions. The rate at which these reactions occur by themselves (i.e., in an environment with only the substrate) is typically too low to maintain life. As a solution, cells produce types of proteins known as enzymes that increase the rate of reaction, a process known as catalyzation. Cells can also use enzymes to breakdown a substrate in the environment into a product that can then be used as a resource. In the next lecture you will learn specific examples of this process, but in order to model this process it is necessary to derive a general function that describes the rate of a reaction driven by an enzyme.

In order to derive this function it is necessary to identify the steps of an enzymatic reaction:

1. The enzyme E attaches to substrate S at rate k_{1+}, forming the complex $\mathrm{E} \cdot \mathrm{S}$

2. The formation of the complex $\mathrm{E} \cdot \mathrm{S}$ can be reversed at rate k_{1-} (typically $k_{1+} \gg k_{1-}$

3. The product P is produced from the complex $\mathrm{E} \cdot \mathrm{S}$ at rate k_2, releasing the enzyme back into the environment while using up the substrate.

In chemistry notation, such a reaction can be written as

$$\mathrm{S} + \mathrm{E} \underset{k_{1-}}{\overset{k_{1+}}{\rightleftharpoons}} \mathrm{E} \cdot \mathrm{S} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

But we are interested in a function for the rate of reaction that produces P, meaning that we are interested in how the *concentration* of P changes with time

$$\frac{d}{dt}[\mathrm{P}] = k_2[\mathrm{E} \cdot \mathrm{S}] \tag{6}$$

where $[\cdot]$ represents the molar concentration of the variable. To solve this equation, we notice that we have a forward and reverse reaction in our initial formula. The formation of the substrate and the complex at steady state can be understood as the ratio of the reaction rates

$$\frac{[\mathrm{E} \cdot \mathrm{S}]}{[\mathrm{E}]_{\mathrm{free}} \cdot [\mathrm{S}]} = \frac{k_{1+}}{k_{1-}} \tag{7}$$

where we have denoted the concentration of free enzyme. We now have a formula for $[\mathrm{E} \cdot \mathrm{S}]$ that we can plug into our ODE. But often we the concentration of the enzyme is more difficult to measure or manipulate than that of the substrate, making it undesirable to retain in our final formula. We can remove this dependency by invoking the *principle of mass balance*, as we are assuming that the experiment is being performed in a closed system.

$$[\mathrm{E}]_{\mathrm{tot}} = [\mathrm{E} \cdot \mathrm{S}] + [\mathrm{E}]_{\mathrm{free}} = [\mathrm{E} \cdot \mathrm{S}] + \frac{[\mathrm{E} \cdot \mathrm{S}]}{[\mathrm{S}]} \frac{k_{1-}}{k_{1+}} \tag{8}$$

which we solve to obtain

$$[\mathrm{E} \cdot \mathrm{S}] = [\mathrm{E}]_{\mathrm{tot}} \frac{[\mathrm{S}]}{[\mathrm{S}] + \frac{k_{1-}}{k_{1+}}} \tag{9}$$

giving us the ODE

$$\frac{d}{dt}[\mathrm{P}] = k_2[\mathrm{E}]_{\mathrm{tot}} \frac{[\mathrm{S}]}{[\mathrm{S}] + \frac{k_{1-}}{k_{1+}}} \tag{10}$$

which we can simplify by defining two *phenomenological* parameters:

1. The limiting rate of reaction for a fixed $[\mathrm{E}]$ as $[\mathrm{S}] \to \infty$, $\mu_{\max} \equiv k_2[\mathrm{E}]_{\mathrm{tot}}$
2. The concentration of substrate at which the reaction rate is half of $\mu_{\max}$, known as the Michaelis constant, $\kappa \equiv \frac{k_{1_-}}{k_{1_+}}$

giving us

$$\mu([\mathrm{S}]) \equiv \frac{d}{dt}[\mathrm{P}] = \mu_{\max}\frac{[\mathrm{S}]}{[\mathrm{S}]+\kappa} \tag{11}$$

You have just derived the *Michaelis–Menten model*, a fundamental and flexible model of enzyme kinetics [5, 6] (see [7] for various flavors of this model). This derivation should feel familiar, as we used a similar approach to obtain a model of logistic growth under a single limiting resource. In addition, the functional form of this model is the same as the Monod equation of growth, meaning that it has the same limiting behavior.

1. Linear rate of reaction when $[\mathrm{S}] \ll \kappa \rightarrow \mu \approx \frac{\mu_{\max}}{\kappa}[\mathrm{S}]$
2. Constant rate of reaction when $[\mathrm{S}] \gg \kappa \rightarrow \mu \approx \mu_{\max}$

References

1. Chesson, P. MacArthur's consumer-resource model. *Theoretical Population Biology* **37,** 26–38. ISSN: 0040-5809. `https://www.sciencedirect.com/science/article/pii/004058099090025Q` (2025) (Feb. 1990).
2. Cui, W., III, R. M. & Mehta, P. *Les Houches Lectures on Community Ecology: From Niche Theory to Statistical Mechanics* arXiv:2403.05497 [q-bio]. Mar. 2024. `http://arxiv.org/abs/2403.05497` (2025).
3. Monod, J. THE GROWTH OF BACTERIAL CULTURES. en. *Annual Review of Microbiology* **3.** Publisher: Annual Reviews, 371–394. ISSN: 0066-4227, 1545-3251. `https://www.annualreviews.org/content/journals/10.1146/annurev.mi.03.100149.002103` (2025) (Oct. 1949).
4. Fink, J. W., Held, N. A. & Manhart, M. Microbial population dynamics decouple growth response from environmental nutrient concentration. *Proceedings of the National Academy of Sciences* **120.** Publisher: Proceedings of the National Academy of Sciences, e2207295120. `https://www.pnas.org/doi/10.1073/pnas.2207295120` (2025) (Jan. 2023).
5. Michaelis, L., Menten, M. L., *et al.* Die kinetik der invertinwirkung. *Biochem. z* **49.** Publisher: Berlin, 352 (1913).
6. Johnson, K. A. & Goody, R. S. The Original Michaelis Constant: Translation of the 1913 Michaelis-Menten Paper. *Biochemistry* **50,** 8264–8269. ISSN: 0006-2960. `https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381512/` (2025) (Oct. 2011).
7. Cornish-Bowden, A. *Fundamentals of enzyme kinetics* 4., completely revised and greatly enlarged ed. eng. ISBN: 978-3-527-33074-4 (Wiley-Blackwell, Weinheim, 2012).

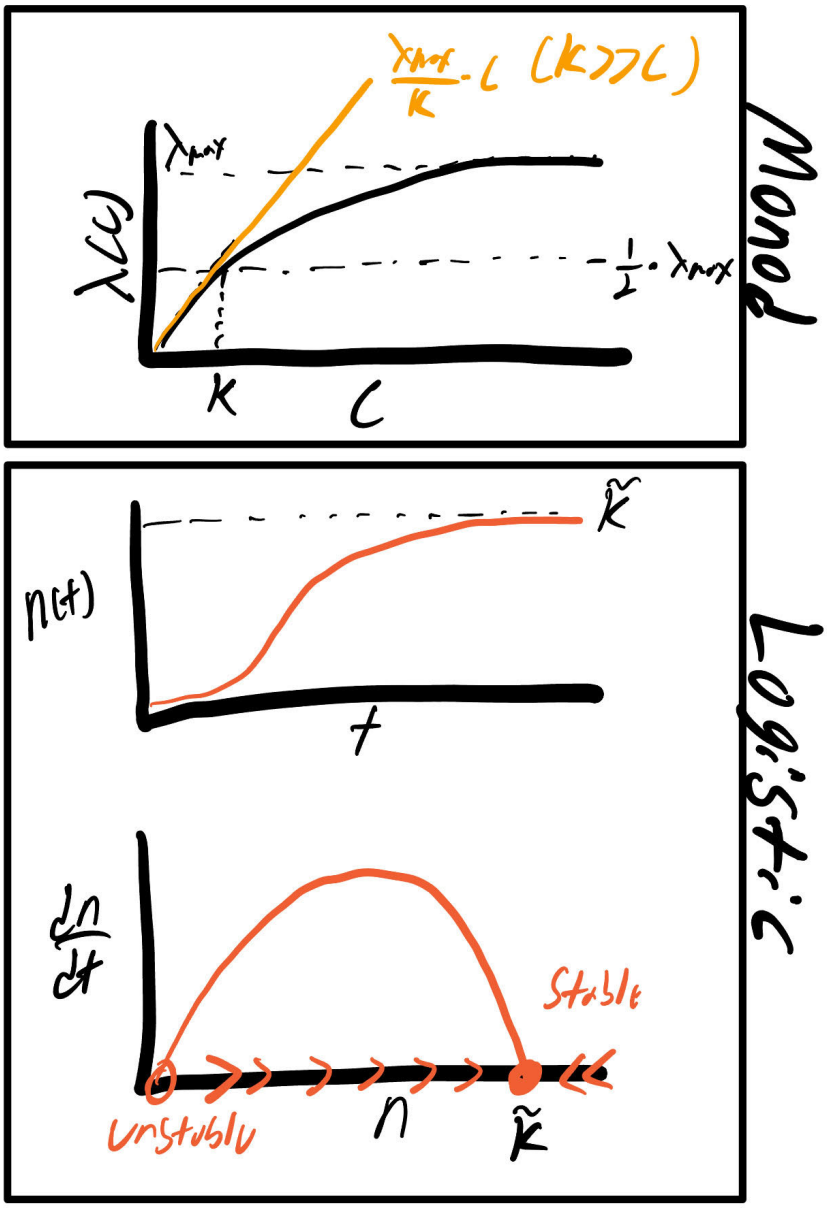

Figure 1: Illustrations of the qualitative behavior of the Monod model of growth rate and the logistic model of growth.