Lecture 4: Microbial growth on a community-produced substrate

William R. Shoemaker

Quantitative Life Sciences, The Abdus Salam International Centre for Theoretical Physics (ICTP), Trieste, 34151, Italy.

September 8, 2025

Constructing the model

In the previous lecture you learned the fundamentals of an experiment where two mutant strains each perform a separate reaction, the product of which is the carbon source source that both strains rely on for growth. In this lecture we will focus on building a minimal model of the system and explore the limiting behavior.

We start with some notation. Ferulic acid (F) gets converted to vanillic acid (V), which then gets converted into a final carbon source, protocatechuic acid, as a substrate for growth (P). We have two mutants: one that cannot perform the $F \to V$ reaction (ΔF) and one that cannot perform the $V \to P$ reaction (ΔV). To simplify the notation, we denote the lower case letter of the variable as the *concentration* (e.g., $f \equiv [F]$). We note that the each of the two reactions are catalyzed by an enzyme produced by a single strain. The dynamics we are interested in capturing with our model are found in Fig 1.

We can try to capture these dynamics by building a system of five ODEs, where resources are depleted and growth ceases after a characteristic saturation timescale t_{sat}. We assume that these enzymes are produced at a rate *proportional to the rate of growth* and that rate of each reaction follows Michaelis–Menten kinetics. In order to apply Michaelis–Menten kinetics we make the following assumptions

1. The concentration of the enzyme-substrate complex is constant (i.e., at steady-state).

2. The concentration of the substrate is much greater than that of the enzyme.

3. Reverse reaction rates are negligible.

1

These assumptions may not strictly hold. For example, we are not providing the intermediate product vanillic acid at the start of the experiment but are providing a small amount of the carbon source. This experimental detail means there is a small period of time where strain ΔV is producing an enzyme for a substrate that is absent. However, the impact of such violations can later be examined by building a larger model, where enzymatic concentrations each have their own ODE.

The enzyme reaction rates are $\mu_i(f) \equiv \mu_i^{\max} \frac{f}{f + \kappa_i}$. The growth rate for each strain is $\lambda_i(p) \equiv \lambda_i^{\max} \frac{p}{p + K_i}$. The constant α_i represents the constant rate of enzyme excretion per-unit growth of a given strain.

$$\frac{df}{dt} = -\mu_{\Delta V}(f)\alpha_{\Delta V}\frac{dn_{\Delta V}}{dt} \tag{1a}$$

$$\frac{dv}{dt} = \mu_{\Delta V}(f)\alpha_{\Delta V}\frac{dn_{\Delta V}}{dt} - \mu_{\Delta F}(v)\alpha_{\Delta F}\frac{dn_{\Delta F}}{dt} \tag{1b}$$

$$\frac{dp}{dt} = \mu_{\Delta F}(v)\alpha_{\Delta F}\frac{dn_{\Delta F}}{dt} - \frac{1}{Y}\left(\frac{dn_{\Delta F}}{dt} + \frac{dn_{\Delta V}}{dt}\right) \tag{1c}$$

$$\frac{dn_{\Delta V}}{dt} = \lambda_{\Delta V}(p)n_{\Delta V} \tag{1d}$$

$$\frac{dn_{\Delta F}}{dt} = \lambda_{\Delta F}(p)n_{\Delta F} \tag{1e}$$

In order to (numerically) solve this model it is necessary to identify appropriate initial conditions. Values of initial values of $f(0)$, $n_{\Delta V}(0)$, and $n_{\Delta F}(0)$ must all be > 0. It is also necessary to provide a small, non-zero value of $p(0)$ ($p(0) \ll f(0)$). This is necessary because we have setup our model so that the rate of enzyme production is proportional to the rate of growth, which remains at zero indefinitely if there are no resources available for growth at the start of the experiment.

Analyzing the behavior of the model

When examining a model with an experiment in mind it is useful to identify the variables that will be measured. In this course you will primarily be measuring *total* community biomass as OD_{600}. We denote OD_{600} as $B(t) \propto n_{\Delta V}(t) + n_{\Delta F}(t)$), meaning that it is proportional to the sum of number of cells of both community members, omitting the constant that converts cells into the measured wavelength. You will also be manipulating 1) the initial total biomass of the community (via inoculation volume) and 2) the initial fraction of ΔF. Therefore, one question worth investigating is how the final total community biomass depends on these two initial conditions. A few example questions:

- Can you use mass conservation to predict how final biomass $B(t_{\text{sat}})$ depends on initial biomass $B(0)$? What is the meaning of the intercept of such a relationship?

- What parameter values are necessary to reproduce the qualitative dynamics in Fig. 1? Numerically solve the system of ODEs using your language of choice (e.g., `solve_ivp()` in Python's `SciPy`).

- Community biomass may not saturate by the end of your experiment depending on your initial conditions and fixed parameters. Identify parameter regimes where the community is continuing to grow at the time of your last measurement. How does this result compare to your experimental observations?

- Vanillic acid can also *inhibit* growth in addition to being a necessary intermediate for the formation of the carbon source [1]. How would you incorporate this detail in the above model?

- Identify three biological features that were ignored in the construction of this model. How would their introduction influence the behavior of this model? Are these features relevant given the design of the experiment?

References

1. Matejczyk, M. *et al.* Biological effects of vanillic acid, *iso*-vanillic acid, and *orto*-vanillic acid as environmental pollutants. *Ecotoxicology and Environmental Safety* **277,** 116383. ISSN: 0147-6513. `https://www.sciencedirect.com/science/article/pii/S0147651324004597` (2025) (June 2024).
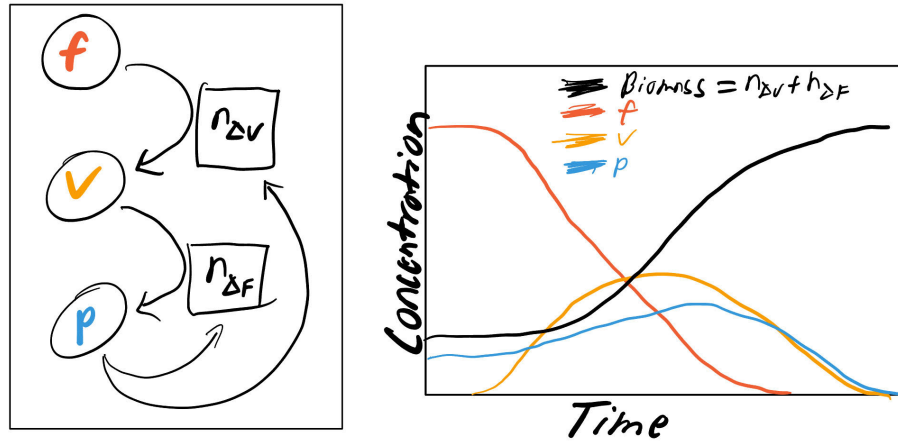
Figure 1: An illustration of the structure of the consumer-resource dynamics of the community and an illustration of the dynamics we suspect occur over the course of the experiment.