# An Introduction to the Mathematics of Bacterial Growth in the Chemostat Bioreactor

*A Foundation Course in Chemostat Modelling*

## Contents of the Course

## Preface

The chemostat is a laboratory device whose mathematical model is physically transparent, analytically tractable, and biologically rich all at once. Its model begins with something modest and visually clear—a pump, a chamber, a bacterial culture, and a nutrient supply—and from this it generates a pair of coupled differential equations whose behaviour ranges from complete extinction to stable coexistence, and whose full analysis from first principles through global stability and bacterial harvest optimisation requires nothing more than calculus, linear algebra, and a single conservation argument.

And beyond its convenience, the chemostat is a genuine piece of the world, existing in laboratories across microbiology, biotechnology, and evolutionary biology; bacteria really do wash out when the pump runs too fast, and populations really do stabilise at the coexistence equilibrium when the parameters permit it. So the mathematics is not a fiction imposed on the biology but a language in which something true about life is being said, and learning to read that language—to see why the equations take the form they do, what every term means, and why the stability analysis comes out the way it does—is learning something about both mathematics and the living world at the same time.

This course is written for anyone who has met ordinary differential equations and wants to understand, fully and from the ground up, how a mathematical model of bacterial growth is built, analysed, and interpreted. It assumes no prior knowledge of biology beyond the elementary idea that bacteria grow by consuming nutrients, no prior knowledge of the chemostat, and everything else is developed here in a careful and unhurried manner, with the derivations shown in full, assumptions named before they are used, and the results interpreted after they are proved.

# 1. The Origins of Continuous Culture Theory

## 1.1. Before the Chemostat: Batch Culture and Its Limitations

For most of the history of experimental microbiology, bacterial growth was studied in what is called *batch culture*, where a fixed volume of nutrient medium is inoculated with bacteria, the flask sealed, and the culture allowed to grow until the nutrients are exhausted, producing one of the most familiar pictures in all of biology—an initial lag phase, an exponential phase, a stationary phase, and finally a decline.

Though batch culture was enormously productive as an experimental tool, it carried a structural limitation that became increasingly frustrating as microbiology matured. In a batch culture, conditions change continuously: nutrients deplete as bacteria grow, metabolic waste products accumulate, the pH drifts, and the composition of the medium at the end of the experiment bears little resemblance to its composition at the beginning. A bacterium growing in the early exponential phase is not growing in the same environment as one growing near stationary phase, even in the same flask. In physiological studies designed to ask what is happening inside a cell under defined, reproducible conditions, this continuous environmental drift was a serious obstacle, since reproducibility demanded steady conditions and batch culture could not provide them.

The conceptual solution was to open the flask—making the culture continuous by supplying fresh medium at a controlled rate and removing spent culture at the same rate, so that the volume of liquid in the chamber remained constant and the system could be driven toward a steady state in which both the bacterial density and the nutrient concentration were time-independent. This idea is so natural in retrospect that it is easy to underestimate the intellectual step it represented; the batch culture paradigm had shaped experimental practice for decades, and the shift to continuous culture was not just a technical modification but a reconception of what the experiments could be.

## 1.2. Monod and the Kinetics of Growth

The mathematical foundation of the chemostat was laid, in large part, by the French biologist Jacques Monod, who in a series of experiments during the 1940s studied how the growth rate of bacteria depended on the concentration of the limiting nutrient in their environment, finding a relationship that was neither linear nor arbitrary. At low nutrient concentrations, the growth rate increased approximately in proportion to the nutrient concentration, while at high concentrations it saturated toward a maximum

value that could not be exceeded regardless of how much more nutrient was supplied.

This behaviour was exactly what Leonor Michaelis and Maud Menten had described in 1913 for the rate of an enzyme-catalysed reaction as a function of substrate concentration. Their analysis, based on the mechanism of reversible enzyme-substrate binding followed by irreversible product release, produced the now-famous Michaelis–Menten equation, in which the reaction rate $v$ at substrate concentration $S$ is

$$v(S) = \frac{v_{\max} S}{K_m + S},$$

where $v_{\max}$ is the maximum reaction rate and $K_m$ is the substrate concentration at which the rate is half its maximum value. Monod recognised that bacterial growth, being ultimately driven by enzymatic reactions inside the cell, should satisfy an analogous relationship, and he proposed the *Monod growth function*

$$\mu(C) = \frac{mC}{a + C},$$

where $C$ is the concentration of the limiting nutrient, $m > 0$ is the maximum per-capita growth rate, and $a > 0$ is the half-saturation constant—the nutrient concentration at which the per-capita growth rate is exactly half its maximum.

The qualitative behaviour of this function encodes the biology that drives the entire chemostat model. When $C$ is very small compared with $a$, the denominator is approximately $a$ and $\mu(C) \approx mC/a$, increasing linearly with nutrient concentration, so growth is directly proportional to nutrient supply and the bacteria are nutrient-limited in the strictest sense. When $C$ is very large compared with $a$, the denominator is approximately $C$ and $\mu(C) \approx m$, independent of $C$, meaning growth has saturated and more nutrient cannot accelerate it. The half-saturation constant $a$ governs the transition between these two regimes: a small value means the bacterium reaches near-maximum growth at low nutrient concentrations, while a large value means the bacterium is sensitive to depletion even at moderate concentrations.

### 1.3. The Invention of the Chemostat

In 1950, working independently and publishing within months of each other, two groups arrived at the continuous culture device that would become known as the chemostat. Jacques Monod, at the Institut Pasteur in Paris, described what he called the *bactogène* in a paper connecting his growth kinetics directly to the steady-state behaviour of a flow-through culture. Almost simultaneously, Aaron Novick and Leo Szilard at the University of Chicago published their own device, which they named the *chemostat*—a contraction of *chemical environment is static*—and it is this name that has persisted.

The key insight shared by both groups was that in a flow-through culture operating at steady state, the growth rate of the bacteria is not a free variable determined by the biology alone but is controlled by the operator through the flow rate. At steady state, bacteria can neither accumulate nor decline and must be growing at exactly the rate at which the flow removes them, so since the removal rate is determined by the dilution rate $D = r/V$—the ratio of volumetric flow rate to chamber volume—the steady-state bacterial growth rate is pinned to $D$, and the operator controls the growth rate of the bacteria by controlling the pump. This was a conceptual and experimental revelation that made it possible, for the first time, to maintain bacteria indefinitely at a prescribed, constant growth rate under stable environmental conditions.

The mathematical theory of the chemostat developed in tandem with the experimental practice, and by the 1970s the model analysed in this course had been studied rigorously by several groups, with its complete stability theory—including the global results that are among its most important features—established. The chemostat became a standard object of study in mathematical biology and ecology, appearing as a prototype for resource-consumer models and as a testing ground for techniques in nonlinear dynamical systems, with its influence extending to epidemic modelling, population dynamics, and evolutionary theory, because the structural features of the model—a growth process competing against a removal process with a threshold parameter determining which wins—kept recurring across all of these fields.

## 2. The Physical Setup and the Meaning of the Variables

### 2.1. The Chemostat as a Physical Device

A chemostat consists of a cylindrical growth chamber of fixed volume $V$, measured in litres. Fresh nutrient medium is pumped continuously into the chamber at a fixed volumetric flow rate $r$, measured in litres per hour—simply the volume of liquid entering the chamber per unit time. Simultaneously, culture is withdrawn from the chamber at the same rate $r$, so the total volume of liquid inside the chamber remains constant at $V$ for all time. The incoming medium is sterile, containing nutrients but no bacteria, and is maintained at a fixed nutrient concentration $C_0$, measured in grams per litre (g/L). The bacteria inside the chamber consume the nutrient as they grow, and both bacteria and residual nutrient are carried out continuously in the exiting flow.

The single most important derived quantity describing the operation of the chemostat is the *dilution rate* $D = \frac{r}{V}$, measured in hours$^{-1}$. Its value is the fraction of the chamber contents replaced per unit time, so that if $D = 0.5\ \mathrm{h}^{-1}$, then half

the chamber volume is exchanged every hour. Its reciprocal, $1/D$, is the mean residence time of a fluid particle inside the chamber—the average time a molecule of liquid spends there before being carried out. The dilution rate is the operator's primary control variable, set by adjusting the pump, and every qualitative feature of the chemostat's long-term behaviour depends critically on its value relative to the biological parameters of the bacterial culture.

### 2.2. Concentrations, Densities, and Total Masses

The two state variables of the chemostat model are the nutrient concentration $C(t)$ and the bacterial density $B(t)$, both measured in grams per litre (g/L) and both functions of time $t$.

The nutrient concentration $C(t)$ is the mass of nutrient per unit volume of chamber liquid at time $t$—a density telling you how much nutrient is packed into each litre, not how much nutrient exists in total in the chamber. The total mass of nutrient inside the chamber at time $t$ is the product of this density and the chamber volume,

$$\text{total nutrient mass} = V \cdot C(t) \quad [\text{g}].$$

Similarly, $B(t)$ is the bacterial mass per unit volume of chamber liquid, and the total bacterial mass inside the chamber is $V \cdot B(t)$.

This distinction between a concentration as a density and a total mass as the product of that density and volume is the reason the derivation of the model equations begins by writing balance equations for total masses $V \cdot C(t)$ and $V \cdot B(t)$, rather than for the concentrations directly. The physical processes of inflow and outflow are naturally expressed as rates of change of total mass—it is mass that flows through the pump, not concentration—and writing the balances in terms of total mass allows each process to be stated as an unambiguous flux. Once the balance is established, division by the constant $V$ yields the equation for the concentration itself.

### 2.3. The Monod Growth Function in the Model

The per-capita growth rate of bacteria in the chemostat is governed by the Monod function introduced in Section 1. In the notation of the model,

$$\mu(C) = \frac{mC}{a + C},$$

where $m > 0$ is the maximum per-capita growth rate ($\text{h}^{-1}$) and $a > 0$ is the half-saturation constant (g/L). For a bacterial density $B(t)$, the total rate at which bacterial mass is produced per unit volume of chamber liquid is $B(t) \cdot \mu(C(t))$, and

over the full chamber volume $V$ the total bacterial production rate is $V \cdot B(t) \cdot \mu(C(t))$ grams of bacteria per hour.

Bacterial growth consumes nutrient, and the rate of nutrient consumption is related to the rate of bacterial production through the *yield constant* $\gamma$, defined as

$$\gamma = \frac{\text{bacterial mass produced}}{\text{nutrient mass consumed}} \quad \left[\frac{\text{g bacteria}}{\text{g nutrient}}\right].$$

By definition, producing one gram of bacteria requires $1/\gamma$ grams of nutrient, so producing bacteria at the total rate $V \cdot B(t) \cdot \mu(C(t))$ requires nutrient at the rate

$$\frac{V \cdot B(t)}{\gamma} \cdot \frac{mC(t)}{a + C(t)} \quad \text{[g nutrient/h]}.$$

The yield constant $\gamma$ is a fixed biological property of the bacterium-nutrient pair, measuring how efficiently the bacterium converts food into biomass. It appears in the model only in the nutrient equation, only in the term describing how quickly the food supply is being consumed, and is entirely absent from the bacterial equation, which asks only how quickly the bacteria themselves are multiplying.

## 3. Deriving the Chemostat Model from First Principles

### 3.1. The Nutrient and Bacterial Balance

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### 3.2. The Complete Chemostat Model

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## 4. Non-Dimensionalising the Chemostat Model

### 4.1. The Purpose of Nondimensionalisation

The five-parameter system (**??**)–(**??**) can be simplified dramatically by rescaling its variables. Nondimensionalisation serves the analysis in at least three ways. It reduces the parameter count, because the five physical parameters $m$, $a$, $C_0$, $D$, $\gamma$ do not all act independently: what matters for the behaviour of the system is not the value of $a$ in isolation, but how $a$ compares to $C_0$; not the value of $m$ in isolation, but how $m$ compares to $D$. Constructing dimensionless ratios from the physical parameters

makes these comparisons the explicit objects of study, and as we shall see, the five parameters collapse into exactly two dimensionless groups, so that every prediction of the model is ultimately a statement about these two numbers alone.

It also makes the variables interpretable. In the physical equations, the statement $C(t) = 0.3$ g/L has meaning only if you already know the scale of the system. In the rescaled equations, the corresponding statement $c(\tau) = 0.3$ means the chamber nutrient concentration is at 30% of the inflow level—a statement with immediate comparative meaning, independent of any particular experimental context.

And it produces what is perhaps least often remarked on but equally consequential—structural legibility. The rescaled equations often reveal symmetries, conservation laws, and structural features hidden in the physical equations. In this chemostat model, the nondimensionalisation will reveal a conservation law, a combination of the two variables satisfying a particularly simple equation on which the entire global stability analysis rests.

### 4.2. Choosing the Rescaling Variables

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### 4.3. Rescaling the Nutrient and Bacterial Equations

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### 4.4. The Dimensionless System and Its Parameters

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## 5. The Equilibrium Points of the Dimensionless System

### 5.1. What an Equilibrium Means

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### 5.2. Computing the Washout Equilibrium

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### 5.3. Computing the Coexistence Equilibrium

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### 5.4. Conditions for Biological Validity

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## 6. Stability Analysis of the Dimensionless System

### 6.1. The Dilution Rate as a Per-Capita Loss Rate

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### 6.2. The Jacobian Matrix of the System

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### 6.3. Local Stability of the Washout Equilibrium

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### 6.4. Local Stability of the Coexistence Equilibrium

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### 6.5. The Conservation Law and Global Stability

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### 6.6. The Complete Stability Picture

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## 7. Optimising the Bacterial Harvest from the Chemostat

### 7.1. The Harvest Rate and Its Dependence on the Dilution Rate

The stability analysis of the previous section established that whenever $D < D_0$, the chemostat settles at the coexistence equilibrium $E_+ = (c^*, b^*)$, with

$$b^* = 1 - \frac{\bar{a}}{\bar{m} - 1}.$$

In the context of biotechnology, where the chemostat is operated not merely to sustain bacteria but to collect them, the relevant quantity is not the steady-state bacterial density $b^*$ alone but the rate at which bacteria are carried out of the chamber by the flow. Since the outflow removes a fraction $D$ of the chamber contents per unit time, the dimensional rate at which bacterial mass leaves the chamber at steady state is

$$\text{harvest rate} = D \cdot B^*.$$

By the conservation identity $c^* + b^* = 1$ from Section 5, which implies $b^* = 1 - c^*$, and with $C = c\,C_0$ and $B = b\,\gamma C_0$,

$$C^* = c^* C_0 = C_0 \left( \frac{\bar{a}}{\bar{m} - 1} \right) = C_0 \left( \frac{a/C_0}{m/D - 1} \right) = \frac{aD}{m - D}$$

$$B^* = b^* \gamma C_0 = (1 - c^*)\gamma C_0 = \gamma(C_0 - c^* C_0) = \gamma(C_0 - C^*)$$

Therefore in physical units, $B^* = \gamma(C_0 - C^*)$, where $C^* = aD/(m - D)$ is the break-even nutrient concentration. Substituting,

$$B^* = \gamma \left( C_0 - \frac{aD}{m - D} \right) = \gamma \cdot \frac{C_0(m - D) - aD}{m - D} = \gamma \cdot \frac{C_0 m - (C_0 + a)D}{m - D}.$$

The dimensional harvest rate is therefore

$$\mathcal{H}(D) = D \cdot B^* = \gamma \cdot \frac{D\big[C_0 m - (C_0 + a)D\big]}{m - D}, \tag{1}$$

a function of $D$ alone, with all other quantities being fixed biological and operational parameters. This function is defined on the interval $(0, D_0)$, below the critical dilution rate, and it is zero at both endpoints: $\mathcal{H}(0) = 0$ because there is no flow, and $\mathcal{H}(D) \to 0$ as $D \to D_0^-$ because $B^* \to 0$ as the bacterial population approaches washout.

Since $\mathcal{H}$ is continuous and positive on the open interval $(0, D_0)$, it must attain a maximum at some interior point $D^* \in (0, D_0)$—the *optimal dilution rate*—the pump setting that maximises the rate of bacterial output.

### 7.2. Finding the Optimal Dilution Rate

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## 8. Chemostat in the Context of Mathematical Biology

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### 8.1. Structural Analogies with Epidemic Models

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### 8.2. The Chemostat as a Resource-Consumer Prototype

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### 8.3. Directions for Further Study

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