# Introduction to the Chemostat

H.T. Banks and Marie Davidian

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North Carolina State University

Raleigh, NC 27695

# The System

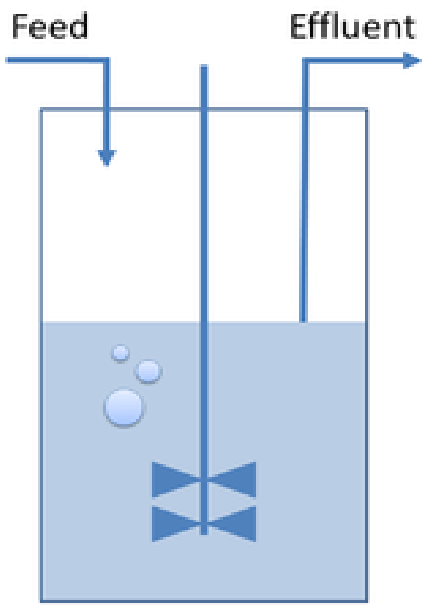


Figure 1: Chemostat schematic.

We consider the problem of growth of micro-organisms, for example, a population of bacteria requiring an energy source containing carbon for growth–(say a simple sugar). Suppose we have some bacteria in a container, and we add nutrients continuously in this container (i.e., a continuous culture medium). Assume the bacteria's growth depends on a limiting nutrient alone (i.e., all other nutrients are in excess and other conditions necessary for their growth are adequate). The container has an outlet so that nutrients and bacteria in the container can flow out. We further assume the container is well mixed. Question is how do we understand the dynamics in the container sufficiently well so as to operate continuously at equilibrium or steady state and what are the steady states, if any? From 1950's, has lead to many investigations [BC, Cap, CN, HHW, Monod, NS, Rub, SW, TL] on modeling of chemostat problems.

Chemostats are also used as microcosms in ecology [BHMJA, PK] and evolutionary biology [WMB, DD, WWE, JE] as well as in wastewater treatment based on chemostat models [BHWW] and has led to numerous patents!!!! . In the some cases, mutation/selection is detrimental, in other cases, it is the desired process under study.

Chemostat dynamics and their understanding have led to many mathematical investigations including those of Wolkowicz and co-authors – see [BW] and 30+ subsequent references–

## The Mathematical Model

Modeling is based on compartmental analysis, laws of mass action, and mass balance. To formalize the problem, we introduce some notation.

- Let $V$ be the volume of the chemostat (the container, and it is fixed in our example) in the unit of liters ($l$).

- Let $Q$ be the volumetric flow rate (flow rate into and out of the chemostat) in unit of liters per hour ($l/hr$).

- Let $q = \frac{Q}{V}$ be the dilution rate in the unit of 1 per hour ($1/hr$); (then $\frac{1}{q}$ is the mean residence time for a particle in the growth chamber).
- Let $N(t)$ be the mass of bacteria at time $t$ in the unit of gram ($g$), $N(t_0) = N_0$.
- Let $c(t)$ be the concentration of rate limiting nutrient in the unit of gram per liters ($g/l$),

$c(t_0) = 0$.

- Let $r$ be the growth rate of the bacteria in units of per hour $(1/hr)$. Assume growth is enzyme mediated (e.g., growth of *E. coli* with nutrient galactose via enzyme galactosekinase). Then one expects $r$ is a function of $c$ ( as we will explain below, we will use Michaelis-Menten/ Briggs-Haldane kinetics for saturation limited growth rates).

We can describe the chemostat with a coupled set of differential equations derived using mass balance and laws of mass action: $(\frac{dm}{dt} \propto \rho(m))$ :

$$\frac{dN(t)}{dt} = r(c(t))N(t) - qN(t)$$
$$\frac{dc(t)}{dt} = qc_0 - qc(t) - \frac{1}{y}r(c(t))N(t).$$

Here the term $qc_0$ represents the input rate, i.e., the rate we add nutrients into the container and $y$ is the yield parameter where $y \propto Y$, where $Y$ is the yield constant defined by

$$Y = \frac{\text{mass of bacteria change/time}}{\text{mass of nutrient consumed/time}}.$$

Typically, $r(c)$ is assumed to have the form

$$r(c) = \frac{R_{max} c}{K_m + c}$$

. So that $r(c)$ can not exceed $R_{max}$ and it will approach $R_{max}$ when $c \to \infty$, i.e., saturation limited kinetics. This is based on Michaelis-Menten/Briggs-Haldane reaction kinetics [BanksLN, BH, MM, Rub]–more later.

## Steady State of the System

We are interested in operating the chemostat under steady state or equilibrium conditions. The chemostat dynamical system for which we wish to find the steady state is

$$\dot{N}(t) = r(c(t))N(t) - qN(t)$$

$$\dot{c}(t) = q(c_0 - c(t)) - \frac{1}{y}r(c(t))N(t),$$

where

$$q = \frac{Q}{V} \text{ and } r(c) = \frac{R_{max}c}{K_m + c}.$$

For this system, we want to find the steady state, i.e., we want to find constants $(\bar{N}, \bar{c})$ such that

$$\left.\frac{dN}{dt}\right|_{(\bar{N},\bar{c})} = 0 \quad \left.\frac{dc}{dt}\right|_{(\bar{N},\bar{c})} = 0.$$

Set

$$r(\bar{c})\bar{N} - q\bar{N} = 0,$$

and to obtain cases of interest assume $\bar{N}$ is non-zero, so dividing, obtain $r(\bar{c}) = q$, can explicitly solve for $\bar{c}$ thus:

$$\frac{R_{max}\bar{c}}{K_m + \bar{c}} = q$$

or $(R_{max} - q)\bar{c} = qK_m$ and hence

$$\bar{c} = \frac{K_m q}{R_{max} - q}.$$

Next, we set

$$q(c_0 - \bar{c}) - \frac{1}{y} r(\bar{c}) \bar{N} = 0,$$

but since $r(\bar{c}) = q$, we see that

$$(c_0 - \bar{c}) - \frac{1}{y} \bar{N} = 0,$$

which means that

$$\bar{N} = y(c_0 - \bar{c}).$$

Thus, to sum up, we see that a nontrivial steady state is given by

$$(\bar{N}, \bar{c}) = \left( y(c_0 - \bar{c}), \frac{K_m q}{R_{max} - q} \right). \qquad (1)$$

Thus, when simulating for Homework 1, a good check to verify the coding has been done correctly is to run the simulation over a long time period and verify that it tends to the steady state. In other words, one should verify that as $t \to \infty$, $N(t) \to \bar{N}$ and $c(t) \to \bar{c}$.

Remark: There also exists a trivial solution to the equilibrium problem, specifically $(\bar{N}, \bar{c}) = (0, c_0)$, which is easily verified from the original system. However, this solution is not of interest to us, as it implies that $N = 0$, which implies that there is no action taking place (it also represents an unstable equilibrium).

We see from (1) that $\bar{c}$ depends on $c_0$, which means for any $c_0$, we will arrive at a different equilibrium, but if we were to *start* at $(\bar{N}, \bar{c})$, we would stay there, and this is true if $(\bar{N}, \bar{c})$ is $(0, c_0)$ or that represented by (1). However, if we start at a point other than an equilibrium, for the (1) equilibria, it will converge to those equilibria, but, as we shall later establish, it will *never* converge to $(0, c_0)$ because by definition $y \neq 0$, and since we started at a point *other than* equilibrium, $c_0 \neq \bar{c}$ therefore, $\bar{N} \neq 0$. Thus we say that $(0, c_0)$ is an *unstable equilibrium* while the nontrivial state $(\bar{N}, \bar{c})$ of (1) is a *stable equilibrium*.

For a discussion of Michaelis-Menten/Briggs-Haldane kinetics, we turn the summary *Brief Review of Enzyme Kinetics*, Chapter 1 of [BanksLN] – see also [Rub].

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