Preface

The dynamic simulation of biological reactors is based on the modeling of a large number of coupled physical and biological phenomena. A predominant feature is the wide range of spatial and temporal scales involved. This modeling is based on the theoretical analysis of the phenomena and, when the techniques exist, on the analysis of experimental data. Research carried out for almost two decades now leads us to consider that turbulent flow, phase transfer, mixing state, biological reactions and the dynamics of microbial populations must be considered with the same interest and simultaneously with the extent of our means.

In the great majority of cases, biological reactors are agitated and/or aerated so that the flow regime is turbulent. However, in the field of reactive turbulent flows, particularly with regard to the respective contributions of fluid mechanics and process engineering, it is difficult to find a better introduction than the one given by Rodney Fox in his book *Computational Models for Turbulent Reacting Flows* [FOX 03].

Here are some excerpts:

> *At first glance, to the uninitiated, the subject of turbulent reacting flows would appear to be relatively simple. Indeed, the basic governing principles can be reduced to a statement of conservation of chemical species and energy... and a statement of conservation of fluid momentum... However, anyone who has attempted to master this subject will tell you that it is in fact quite complicated. On the one hand, in order to understand how the fluid flow affects the chemistry, one must have an excellent*

understanding of turbulent flows and of turbulent mixing. On the other hand, given its paramount importance in the determination of the types and quantities of chemical species formed, an equally good understanding of chemistry is required. Even a cursory review of the literature in any of these areas will quickly reveal the complexity of the task. Indeed, given the enormous research production in these areas during the twentieth century, it would be safe to conclude that no one could simultaneously master all aspects of turbulence, mixing, and chemistry.

Given their complexity and practical importance, it should be no surprise that different approaches for dealing with turbulent reacting flows have developed over the last 50 years. On the one hand, the chemical reaction engineering (CRE) approach came from the application of chemical kinetics to the study of chemical reactor design. In this approach, the details of the fluid flow are of interest only in as much as they affect the product yield and selectivity of the reactor. In many cases, this effect is of secondary importance, and thus in the CRE approach, greater attention has been paid to other factors that directly affect the chemistry. On the other hand, the fluid-mechanical (FM) approach developed as a natural extension of the statistical description of turbulent flows. In this approach, the emphasis has been primarily placed on how the fluid flow affects the rate of chemical reactions. In particular, this approach has been widely employed in the study of combustion...

In hindsight, the primary factor in determining which approach is most applicable to a particular reacting flow is the characteristic time scales of the chemical reactions relative to the turbulence time scales...

We recommend a thorough reading of this introduction and the first chapter which show how to establish a comprehensive dialogue between the two approaches. Naturally, our contribution will be much more modest but with an identical inspiration. Thus, in the first part of this work devoted to a synthesis of the various problems to be considered, we will use notions relating to process engineering, fluid mechanics, statistics and microbiology with the aim of highlighting convergence points. It will also be shown that each discipline meets its limits and the different views of each discipline

make it possible to better understand the questions that are now receiving special attention in research.

We will then have the relationships of the characteristic times for the physical and chemical phenomena or biological phenomena; we will have approaches derived from fluid mechanics, reactor engineering and then from biology with all of its specificities. Among those, we can already emphasize that the particularity of bioprocesses (in relation to chemical processes) lies in what connects the living with the physical world, which are exchanges across the membrane.

In the introductory text of Rodney Fox, we can note the very close proximity between biological reactions and combustion. A fuel is a substance that, in the presence of oxygen and energy, can combine with oxygen (which acts as an oxidant) in a chemical reaction that generates heat: combustion. The parallel is obvious, even if it means using analogy, which is the weakest of logical arguments. The cell or microorganism, by virtue of its ability to produce energy, catalyzes the combustion of the carbonaceous substrate and oxygen which it collects from its environment. Feeding the cellular motor involves bringing fuel and oxidant to the cell and then passing them through the membrane, from the physical to the living. The two phenomena are necessarily consecutive: just as the mixture precedes the reaction, assimilation[1] is intercalated between these two in the case of microbiology. This interface, the membrane, which allows the internal biochemistry to be freed from the strict contingency of thermodynamics, constitutes a major interest for those studying the functioning of biological systems and their industrial applications. This singularity of the living being consisting of using the energy of intracellular reactions to control the transfer between the outside and the inside poses new difficulties compared to the case of chemical systems. While temperature, pressure and composition were sufficient to determine a rate of chemical reaction, it is necessary, in the case of bioreactions, to take into account the state of the cells. Everything would be only a little more complicated if the "state equations" of biological systems were known. However, the information at this level is often global averaged and we do not have local equations that are exact at the cell's scale, which can then be coupled with the flow and integrated to return to the scale of an elementary volume. On the contrary, the number of quantities required to determine the state of a microorganism is considerable. These difficulties

1 In other words, the transfer of matter between liquid phase and biological phase.

are at the heart of the modeling work for anyone who intends to couple hydrodynamics and biological reactions.

What else should be added to conclude this introduction? Beyond the order in which the various points (flows, transfers, bioreactions and mixing) will be approached, the last dimension relates to taking into account the notion of population, the diversity of states within the same population, the ability to remain outside the equilibrium with the external environment and the plasticity of the network of intracellular reactions. An important part will be devoted to the implementation of biological population balance and will propose, after a bibliographic synthesis, more forward-looking aspects.

It might seem obvious to use the concept of population balance in the study of biological systems and yet the number of works using the notion of population balance applied to bioprocesses remains low[2] (<1,000) whereas it exceeds 100,000 in the field of process engineering alone. There is therefore still much to be integrated, if not, to be invented in the field.

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2 Work in the field of medicine and mathematics should be included in order to be more realistic.