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Publication date:
2015

Document Version
Publisher's PDF, also known as Version of record

HYDRODYNAMIC CHARACTERIZATION OF SUBSTRATE GRADIENTS IN A PILOT SCALE FERMENTER USING CFD AND SPATIALLY DISTRIBUTED SENSORS

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INTRODUCTION

The prediction and understanding of mixing and oxygen mass transfer in fermenters and bioreactors is useful for bioprocess improvement as these dynamics govern production rates of the biotransformation. In particular heterogeneities occurring under process conditions is of interest as such gradients present challenges for process development and scale up [1]. Heterogeneities in substrate concentration have been identified in large scale fermenters [2] and reliable tools to identify and quantify these phenomena are required. This work utilizes the degradation of hydrogen peroxide to oxygen by catalase to illustrate and validate how substrate is distributed throughout the vessel by combining CFD and experimental data collected with spatially distributed sensors.

ENZYME KINETICS AND MIXING CHARACTERIZATION

The reaction kinetics are gathered from experiments in a stirred batch reactor with a working volume of 200 mL at 25 OC, and with an agitation speed of 300 rpm. The production rate of oxygen was measured using a PyroScience optical fiber sensor system. The reaction kinetics was modelled by standard Mechaelis Menten kinetics shown in (Figure 2).

$$2H_2O_2 \xrightarrow{Catalase} O_2 + 2H_2O$$

The mixing was characterized (Figure 1), in a continuously stirred 700 L pilot-scale reactor fitted with a single Rushton impeller, by tracer experiments using sodium chloride pulses. The conductivity was measured at multiple locations in the vessel using in house conductivity sensors. The mixing time was determined as the time to reach 95 % of the final steady state conductivity value. The CFD simulations were carried out, in ANSYS CFX® 16, with similar conditions as the experiments, while using shear stress transport to account for turbulence.

MIXING CHARACTERISTICS

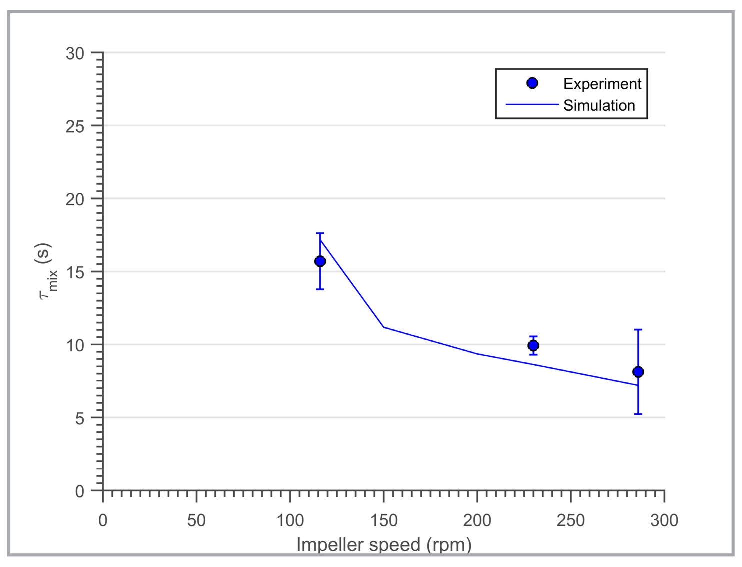

Figure 1: Validation of simulated hydrodynamics through mixing time in the 700 L vessel agitated at different velocities.

REACTION KINETICS

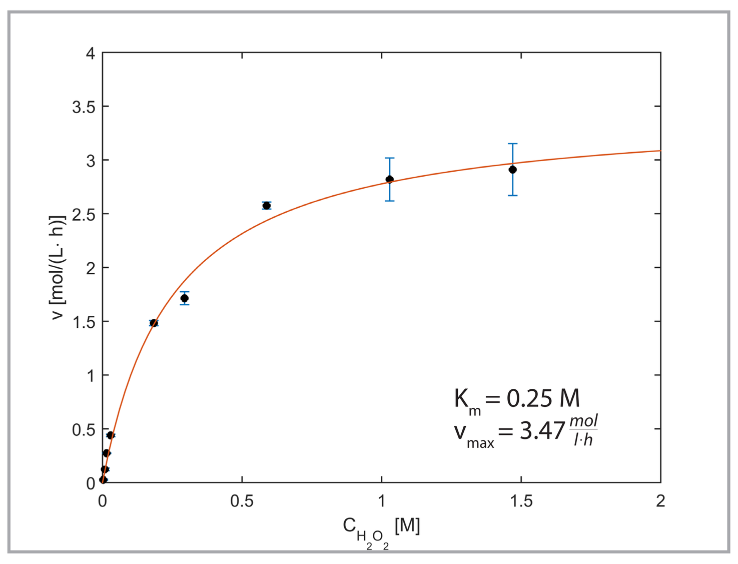

Figure 2: Initial rate of oxygen production as a function of hydrogen peroxide concentration. The red curve show the Michaelis Menten kinetic model prediction with fitted parameters.

$$v = v_{max} \cdot \frac{[H_2O_2]}{K_m + [H_2O_2]}$$

SUBSTRATE AND PRODUCT GRADIENTS

The occurrence of gradients in hydrogen peroxide and dissolved oxygen concentration was investigated in a 700 L continuously stirred pilot scale bioreactor fitted with one Rushton turbine at 230 rpm. A CFD model was validated in terms of dissolved oxygen measurement acquired at four different locations along the height of the reactor. The substrate gradients indicate different profiles of dissolved oxygen depending on the kLa distribution in the vessel. Different oxygen transfer coefficient profiles were investigated and the best representation of the data was identified by applying a uniform kLa throughout the tank in the model (Figure 3).

DISSOLVED OXYGEN PROFILE

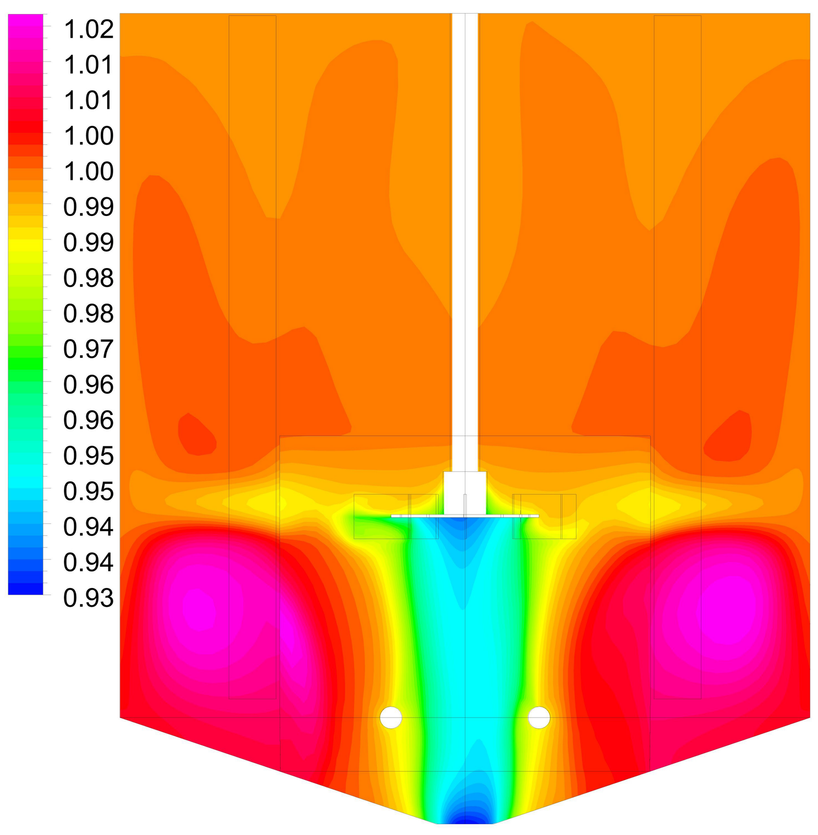

Figure 3: Scaled oxygen concentration in the vessel at 230 rpm, where the kLa was assumed to be uniformly distributed

MODEL VALIDATION

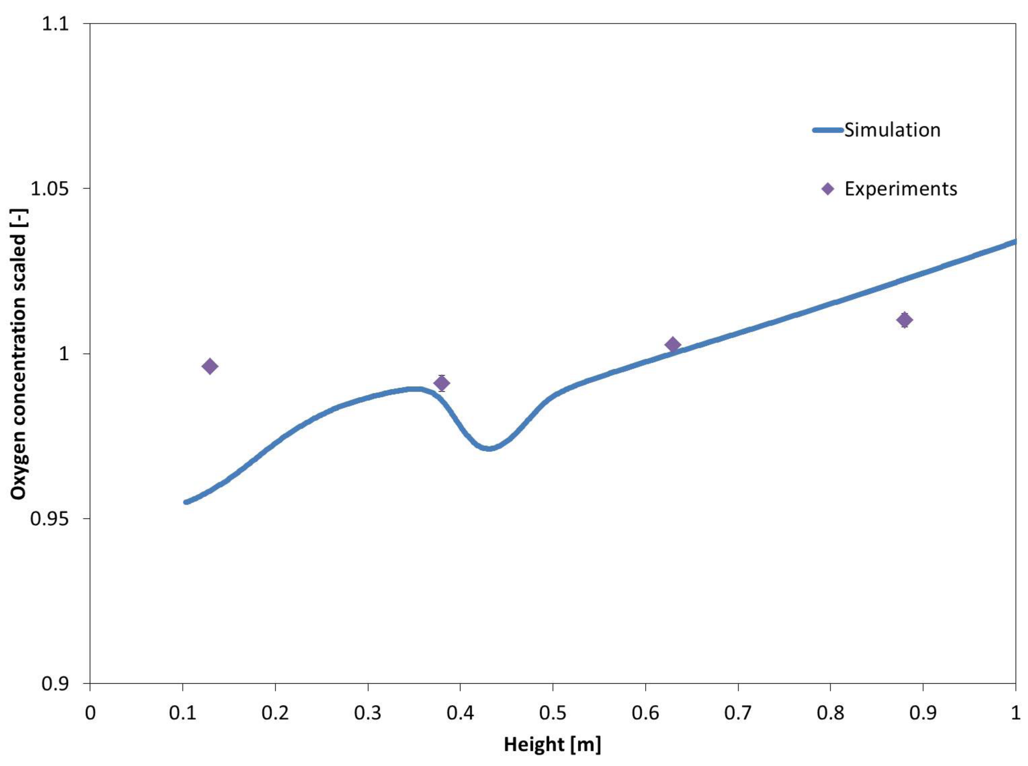

Figure 4: The oxygen concentration as a function of reactor height. The experimental values represent the output of four different sensors.

HYDROGEN PEROXIDE PROFILE

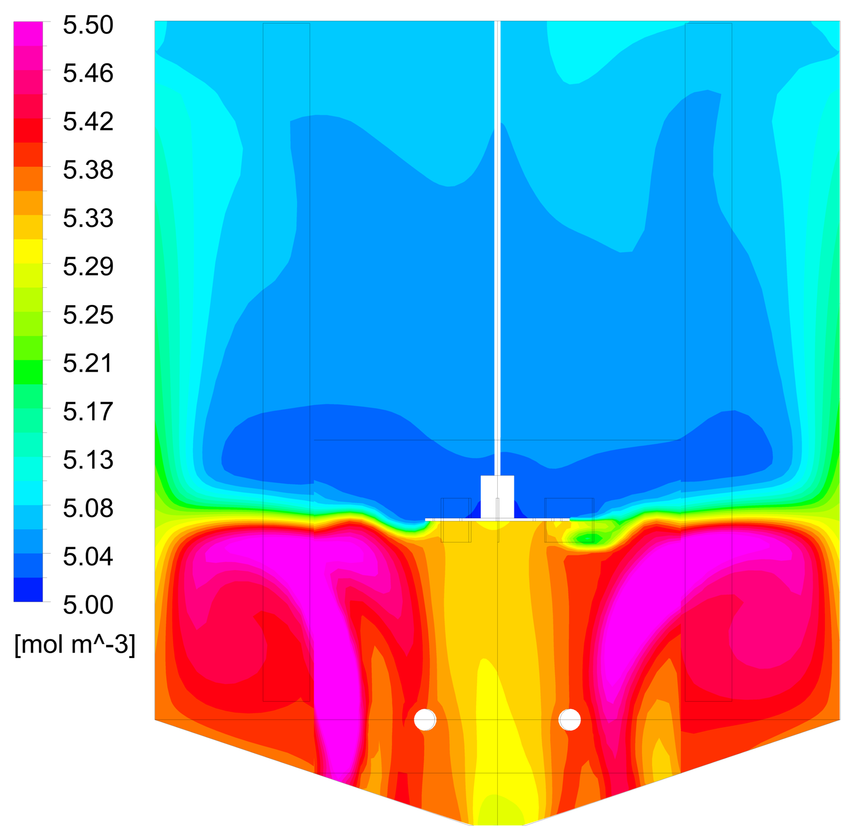

Figure 5: Predicted hydrogen peroxide concentration throughout the tank based on the investigated reaction kinetics and dosing position.

Comparing with experimental data, and for the experimental conditions applied, the average kLa profile shows the best fit to the data (Figure 4). This indicates that the measured differences in oxygen concentrations are caused by substrate gradients (Figure 5) and poor mixing and not by differences in mass transfer.

CONCLUSION AND FUTURE WORK

The characterization method applied in this work was able to provide a strong indication on the distribution of mass transfer coefficients in a stirred pilot-scale bioreactor by combining reaction kinetics and computational fluid dynamics. The use of spatially distributed sensors is essential for this characterization since this is the method used here for validating 3D CFD simulations. Following this work other biological systems will be characterized using other spatially distributed sensors, for example pH, in combination with CFD and detailed understanding of reaction kinetics

ACKNOWLEDGEMENT

The PhD project of Christian Bach has received funding from the Technical University of Denmark (DTU), Novozymes A/S and Innovation Fund Denmark in the frame of the Strategic Research Center BIOPRO2 (BIO-based PROduction: TOwards the next generation of optimized and sustainable processes).

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